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   $0.19  Estimated cost File1
       FTSNET   0.002 Hrs.
   $0.19  Estimated cost this search
   $0.19  Estimated total session cost   0.059 DialUnits

File 155:MEDLINE(R)  1966-1999/Apr W1
    (c) format only 1999 Dialog Corporation

    Set  Items  Description
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? s py=1993:1999
    S1 2337031  PY=1993:1999
? s aav or adeno(w)associated
         504  AAV
        1472  ADENO
      615857  ASSOCIATED
         680  ADENO(W)ASSOCIATED
    S2    761  AAV OR ADENO(W)ASSOCIATED
? s s2 or adenoassociated
         761  S2
          17  ADENOASSOCIATED
    S3    770  S2 OR ADENOASSOCIATED
? s specific?
    S4 867589  SPECIFIC?
? s s3 and s4
         770  S3
      867589  S4
    S5    222  S3 AND S4
? s s5 not s1
         222  S5
     2337031  S1
    S6     73  S5 NOT S1
? t s6/7/6 8 9 14 18 24 36

 6/7/6
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07333400  93043547
 Adeno-associated virus vectors.
 Carter BJ
 Targeted Genetics Corporation, Seattle, Washington.
 Curr Opin Biotechnol (ENGLAND)  Oct 1992,  3 (5) p533-9,  ISSN 0958-1669
Journal Code: A92
 Languages: ENGLISH
 Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
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Adeno-associated virus is a human parvovirus that integrates its DNA genome into host cell chromosomes with very high efficiency. This suggests that adeno-associated virus may be a useful vector for human gene therapy. Interest in adeno-associated virus vectors increased greatly in the last year following reports that adeno-associated virus genome integration may be site specific and occur at preferred sites in the human genome. Several genes relevant to the treatment of genetic or infectious diseases have been expressed in adeno-associated virus vectors in vitro. (51 Refs.)

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 6/7/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07296175  92410609
 Modulation of the cellular phenotype by integrated adeno-associated
virus.
 Winocour  E; Puzis L; Etkin S; Koch T; Danovitch B; Mendelson E; Shaulian
E; Karby S; Lavi S
 Department of Molecular Genetics and Virology, Weizmann Institute of
Science, Rehovot, Israel.
 Virology (UNITED STATES)  Sep 1992,  190 (1) p316-29,  ISSN 0042-6822
Journal Code: XEA
 Contract/Grant No.: AI-26122, AI, NIAID
 Languages: ENGLISH
 Document type: JOURNAL ARTICLE
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The adeno-associated virus (AAV) rep gene encodes a series of overlapping, multifunctional, nonstructural proteins (Rep proteins) which regulate the viral life cycle and which are also capable of trans-regulating nonviral gene expressions (reviewed in Berns, 1990, Microbiol. Rev. 54, 316-329). To investigate the expression of the AAV rep gene in a cellular chromosomal context, SV40-transformed Chinese hamster embryo (OD4) cells were infected with an AAV/neo hybrid virus and progeny resistant to the antibiotic G418 were selected and amplified. Chromosomal integration and RNA transcription of the AAV and neo DNA inserts were confirmed by Southern and Northern blotting procedures. One of the G418R cell lines stably expressed a protein which reacted specifically with AAV anti-Rep antiserum in Western immunoblots. The stable integration of AAV rep DNA, which did not interfere with cell proliferation under normal growth conditions, was associated with two changes in cellular phenotype: eight of nine lines were markedly more sensitive to UV light (254 nm) than were the parental OD4 cells; and seven of the nine lines had lost the capacity to promote SV40 origin DNA amplification in vitro, in contrast to the parental OD4 cells. OD4 cells transformed to G418R by AAV/neo DNA constructs with a deleted rep gene, or by a neo DNA construct lacking AAV DNA, did not display these phenotypic changes. It is suggested that stable integration of the AAV rep gene interferes with cellular processes connected with DNA repair and gene amplification.

6/7/9
DIALOG(R)File 155:MEDLINE(R)

07288855 92287906
Gene transfer in human lymphocytes using a vector based on adeno-associated virus.
Muro-Cacho CA; Samulski RJ; Kaplan D
Institute of Pathology, Case Western Reserve University, Cleveland, Ohio 44106.
J Immunother (UNITED STATES) May 1992, 11 (4) p231-7, ISSN 1053-8550 Journal Code: AZ0
Contract/Grant No.: AI-28923, AI, NIAID; DK-42701, DK, NIDDK; AI-25530, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Adeno-associated virus is a nonpathogenic, dependent parvovirus that integrates at a specific site in human chromosome 19. We have used the inverted terminal repeats of the virus, which mediate integration, to establish a vector for gene transfer in human lymphocytes. A neomycin resistance gene has been stably introduced into nontransformed human T-cell clones and a subsequent analysis of the functional properties of the infected clone revealed no detectable alterations. Rescue and replication of the wild-type virus was accomplished with adenovirus superinfection; however, the vector was not rescued and did not replicate by this procedure, indicating the stability of the integrated vector and demonstrating an additional level of safety incorporated in its construction. An adeno-associated virus-based vector represents an alternative to retroviruses for gene therapy in lymphocytes.

6/7/14
DIALOG(R)File 155:MEDLINE(R)

06954089 92037558
Targeted integration of adeno-associated virus (AAV) into human chromosome 19 [published erratum appears in EMBO J 1992 Mar;11(3):1228]
Samulski RJ; Zhu X; Xiao X; Brook JD; Housman DE; Epstein N; Hunter LA
Department of Biological Sciences, University of Pittsburgh, PA 15260.
EMBO J (ENGLAND) Dec 1991, 10 (12) p3941-50, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI 25530-03, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A key feature in adeno-associated virus (AAV) replication is efficient integration of the viral genome into host cell DNA to establish latency when helper virus is absent. The steps involved in this process remain largely uncharacterized, even though AAV integration was first documented 20 years ago. Using a protein--DNA binding method we isolated AAV--cellular junction DNA sequences. The cellular component hybridized to a single restriction fragment in the virus-free parental cell line, and also co-migrated with AAV-specific sequences in numerous latently infected cell lines. Analysis of somatic cell hybrids indicated that this cellular sequence maps to the distal portion of the q arm of human chromosome 19. In situ hybridization of AAV DNA to chromosomes from latently infected cells confirms the physical location of AAV integrations to be q13.4-ter of chromosome 19. Sequence analysis of several independent integration sites shows breakpoints occurring within a 100 bp cellular region. This non-pathogenic parvovirus thus appears to establish viral latency by integrating its DNA specifically into one chromosomal region. Such specific integration is so far unique among the eukaryotic DNA viruses. The incorporation of site-specific integration into AAV vector schemes should make this vector system attractive for human gene therapy approaches.

6/7/18
DIALOG(R)File 155:MEDLINE(R)

06829588 92052179
Isolation of a candidate repressor/activator, NF-E1 (YY-1, delta), that binds to the immunoglobulin kappa 3' enhancer and the immunoglobulin heavy-chain mu E1 site.
Park K; Atchison ML
Department of Animal Biology, University of Pennsylvania, School of Veterinary Medicine, Philadelphia 19104.
Proc Natl Acad Sci U S A (UNITED STATES) Nov 1 1991, 88 (21) p9804-8, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: RO1 GM42415, GM, NIGMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have determined that the developmental control of immunoglobulin kappa 3' enhancer (kappa E3') activity is the result of the combined influence of positive- and negative-acting elements. We show that a central core in the kappa E3' enhancer is active at the pre-B-cell stage but is repressed by flanking negative-acting elements. The negative-acting sequences repress enhancer activity in a position- and orientation-independent manner at the pre-B-cell stage. We have isolated a human cDNA clone encoding a zinc finger protein (NF-E1) that binds to the negative-acting segment of the kappa E3' enhancer. This protein also binds to the immunoglobulin heavy-chain enhancer mu E1 site. NF-E1 is encoded by the same gene as the YY-1 protein, which binds to the adeno-associated virus P5 promoter. NF-E1 is also the human homologue of the mouse delta protein, which binds to ribosomal protein gene promoters. The predicted amino acid sequence of this protein contains features characteristic of transcriptional activators as well as transcriptional repressors. Cotransfection studies with this cDNA indicate that it can repress basal promoter activity. The apparent dual function of this protein is discussed.

6/7/24
DIALOG(R)File 155:MEDLINE(R)

06626755 90192777
Site-specific integration by adeno-associated virus.
Kotin RM; Siniscalco M; Samulski RJ; Zhu XD; Hunter L; Laughlin CA; McLaughlin S; Muzyczka N; Rocchi M; Berns KI
Hearst Microbiology Research Center, Department of Microbiology, Cornell University Medical College, New York, NY 10021.
Proc Natl Acad Sci U S A (UNITED STATES) Mar 1990, 87 (6) p2211-5, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: AI22251, AI, NIAID; GM37090, GM, NIGMS; AI25530, AI, NIAID; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Cellular sequences flanking integrated copies of the adeno-associated virus (AAV) genome were isolated from a latently infected clonal human cell line and used to probe genomic blots derived from an additional 21 independently derived clones of human cells latently infected with AAV. In genomic blots of uninfected human cell lines and of primary human tissue, each flanking-sequence probe hybridized to unique bands, but in 15 of the 22 latently infected clones the flanking sequences hybridized not only to the original fragments but also to a total of 36 additional species. AAV probes also hybridized to 22 of these new bands, representing 11 of the 15 positive clones, but never to the fragment characteristic of uninfected cell DNA. From these data we conclude that the AAV genome preferentially integrates into a specific region of the cellular genome. We have determined that the integration site is unique to chromosome 19 by somatic cell hybrid mapping, and this sequence has been isolated from uninfected human DNA.

6/7/36
DIALOG(R)File 155:MEDLINE(R)

06116071 87036912
Latent infection of KB cells with adeno-associated virus type 2.
Laughlin CA; Cardellichio CB; Coon HC
J Virol (UNITED STATES) Nov 1986, 60 (2) p515-24, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: R01 AI/CA 19934, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Adeno-associated virus (AAV) is a prevalent human virus whose replication requires factors provided by a coinfecting helper virus. AAV can establish latent infections in vitro by integration of the AAV genome into cellular DNA. To study the process of integration as well as the rescue of AAV replication in latently infected cells after superinfection with a helper virus, we established a panel of independently derived latently infected cell clones. KB cells were infected with a high multiplicity of AAV in the absence of helper virus, cloned, and passaged to dilute out input AAV genomes. AAV DNA replication and protein synthesis were rescued from more than 10% of the KB cell clones after superinfection with adenovirus type 5 (Ad5) or herpes simplex virus types 1 or 2. In the absence of helper virus, there was no detectable expression of AAV-specific RNA or proteins in the latently infected cell clones. Ad5 superinfection also resulted in the production of infectious AAV in most cases. All mutant adenoviruses tested that were able to help AAV DNA replication in a coinfection were also able to rescue AAV from the latently infected cells, although one mutant, Ad5hr6, was less efficient at AAV rescue. Analysis of high-molecular-weight cellular DNA indicated that AAV sequences were integrated into the cell genome. The restriction enzyme digestion patterns of the cellular DNA were consistent with colinear integration of the AAV genome, with the viral termini present at the cell-virus junction. In addition, many of the cell lines appeared to contain head-to-tail concatemers of the AAV genome. The understanding of the integration of AAV DNA is increasingly important since AAV-based vectors have many advantages for gene transduction in vitro and in vivo.
? ds

Set	Items	Description
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S3	770	S2 OR ADENOASSOCIATED
S4	867589	SPECIFIC?
S5	222	S3 AND S4
S6	73	S5 NOT S1

? s promoter or promoters
58468 PROMOTER
14862 PROMOTERS
S7 63088 PROMOTER OR PROMOTERS
? s s3 and s7 not s1
770 S3
63088 S7
2337031 S1
S8 49 S3 AND S7 NOT S1
? s s8 not s6
49 S8
73 S6
S9 33 S8 NOT S6
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9/7/4
DIALOG(R)File 155:MEDLINE(R)

07382011 92348451
Chromosomal localization and organization of the murine genes encoding the beta subunits (AIC2A and AIC2B) of the interleukin 3, granulocyte/macrophage colony-stimulating factor, and interleukin 5 receptors.
Gorman DM; Itoh N; Jenkins NA; Gilbert DJ; Copeland NG; Miyajima A
Department of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, California 94304.
J Biol Chem (UNITED STATES) Aug 5 1992, 267 (22) p15842-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: NO1-CO-74101, CO, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Chromosomal genes for two mouse homologous beta subunits (AIC2A and AIC2B) of the interleukin-3, granulocyte/macrophage colony-stimulating factor, and interleukin-5 receptors were characterized. Both AIC2A and AIC2B genes were present on a 250-kilobase MluI restriction fragment and were mapped on murine chromosome 15 (these loci were provisionally designated as Il3rb-1 (AIC2A) and Il3rb-2 (AIC2B)), closely linked to the c-sis locus. Both genes consist of 14 exons and span about 28 kb each. The major transcription initiation sites of both genes were mapped at 194 bp from the initiation codon. These genes are 95% identical up to 700 bp from the transcription initiation sites. Potential recognition sequences for hemopoietic transcription factors including GATA-1 and PU.1 in addition to a TATA-like sequence are present in the 5'-flanking region. A stretch of 20 bp including the initiation site is homologous to the corresponding region of the erythropoietin receptor and the interleukin-7 receptor genes and to the initiator sequence of the adeno-associated virus P5 promoter, suggesting a possible role in transcription initiation. Comparison of the exon/intron boundaries of AIC2A and AIC2B genes with those of other members of the cytokine receptor superfamily reveals a conserved evolutionary structure. Isolation of various forms of AIC2 cDNAs reveals differential splicing of the transcripts.

9/7/5
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07330679 90329218
The recombinant human parvoviruses for gene therapy of hemoglobinopathies.
Dixit M; Tillery MK; Plonk SG; Ohi S
Department of Biochemistry, Meharry Medical College, Nashville, TN 37208.
SAAS Bull Biochem Biotechnol (UNITED STATES) Jan 1990, 3 p63-8, Journal Code: ALK
Contract/Grant No.: HL01989, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Towards a goal of using adeno-associated viruses (AAV), the human parvovirus, as the gene transfer vector for gene therapy of hemoglobinopathies, the human beta-globin (h beta G) cDNA was ligated downstream of the P40 promoter of AAV type 2 (AAV2) genome. Transfection via electroporation of the construct into human 293 cells (embryonal kidney cell line) resulted in expression of the cloned h beta G cDNA, as evidenced by the synthesis of transcripts hybridizable to h beta G probe. The transfection led to the recombinant genome to be excised out of the plasmid and replicate in the cell, followed by production of the recombinant AAV that harbors h beta G cDNA.

9/7/6
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07302580 93099882
Characterization of a preferred site on human chromosome 19q for integration of adeno-associated virus DNA by non-homologous recombination.
Kotin RM; Linden RM; Berns KI
Molecular Hematology Branch, National Institutes of Health, Bethesda, MD 20892.
EMBO J (ENGLAND) Dec 1992, 11 (13) p5071-8, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI 22251, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The human parvovirus, adeno-associated virus (AAV), has been shown to integrate preferentially into human chromosome 19 q13.3-qter. The human target sequence for AAV integration (AAVS1) was cloned and sequenced. By analysis of the proviral junctions it was determined that integration of the AAV DNA occurred via a non-homologous recombination pathway although there were either four or five identical nucleotides at the junctions. Integration was a multistep, concerted process that resulted in cellular sequence rearrangements. The sequence of the integration locus was analyzed for possible recombination signals. Direct repeats at a much greater than random occurrence were found distributed non-uniformly throughout the AAVS1 sequence. A CpG island containing transcription factor binding site elements is suggestive of a TATA-less promoter. Evidence for transcriptional activity was provided by PCR amplification of reverse transcribed RNA.

9/7/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07295326 92392571
Gene expression from adeno-associated virus vectors in airway epithelial cells.
Flotte TR; Solow R; Owens RA; Afione S; Zeitlin PL; Carter BJ

Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.
Am J Respir Cell Mol Biol (UNITED STATES) Sep 1992, 7 (3) p349-56, ISSN 1044-1549 Journal Code: AOB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Lung diseases such as cystic fibrosis (CF) might be treated by gene therapy using viral vectors delivered to the airway. One potential vector is the defective human parvovirus, adeno-associated virus (AAV). We examined the AAV p5 transcription promoter for gene expression in immortalized cell lines derived from the airway (IB3-1) or pancreas (CFPAC-1) of CF patients. AAV vectors expressing the prokaryotic genes cat (pAAVp5cat) or neo (pAAVp5neo) from the p5 promoter were evaluated after introduction into IB3-1 or CFPAC-1 cells by lipofection. In transient assays in both cell lines, the cat gene was expressed 5- to 10-fold more efficiently from the p5 promoter than from a simian virus 40 early gene promoter (pSVcat). IB3-1 cells were transformed stably to geneticin resistance by pAAVp5neo at a 5-fold higher efficiency than by an SVneo vector. The AAV inverted terminal repeat (ITR) region immediately upstream of the p5 promoter appears to have an enhancer effect and the promoter also contains a CREB site which confers a response to forskolin. In IB3-1 cells, expression of the cat gene from a p5 promoter was decreased about 5-fold by deletion of both the upstream ITR and the CREB site. The AAVp5neo vector was also packaged into AAV particles and used to infect IB3-1 cells as a transducing virus. Under these conditions, 60 to 70% of the cells could be stably transformed to geneticin resistance. Thus, AAV transducing vectors appear to be a highly efficient delivery system for stable integration and expression of genes in cultured airway epithelial cells.

9/7/12
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
06952402 92009221
Construction and expression of a recombinant adeno-associated virus that harbors a human beta-globin-encoding cDNA.
Dixit M; Webb MS; Smart WC; Ohi S
Department of Biochemistry, School of Medicine, Meharry Medical College, Nashville, TN.
Gene (NETHERLANDS) Aug 15 1991, 104 (2) p253-7, ISSN 0378-1119 Journal Code: FOP
Contract/Grant No.: HL019898, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Towards a goal of using recombinant adeno-associated viruses (AAV) for the gene therapy of hemoglobinopathies we had previously constructed plasmid pAV h beta G psi 1, which contained a human beta-globin-encoding cDNA (HBB) downstream from the P40 promoter of AAV2 DNA [Ohi et al., Gene 89 (1990) 279-282]. Transfection of the plasmid into human 293 cells (embryonal kidney cell line) resulted in the expression of HBB at the mRNA level as well as rescue and replication of the recombinant AAV genome (Ohi et al., ibid.). The present study demonstrates that the replicated recombinant DNA was packaged into an intact virion by transcomplementation with pAV2 or the defective helpers, pAV delta Bam or pAVXB. The recombinant virus could be isolated by equilibrium CsCl density gradient, the density of which was about 1.4 g/cm3. The defective helpers are used to produce wild-type AAV-free recombinant AAV. The recombinant AAV were infectious and expressed chimeric mRNAs containing the HBB sequence in virus-infected 293, KB (oral epidermoid carcinoma cell line) and K562 (human erythroleukemia cell line) cells. The importance of the infectivity and expression of the recombinant AAV in hematopoietic cells is discussed in the context of gene therapy of hemoglobinopathies.

9/7/16
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
06634298 90323629
Construction and replication of an adeno-associated virus expression vector that contains human beta-globin cDNA.
Ohi S; Dixit M; Tillery MK; Plonk SG
Department of Biochemistry, School of Medicine, Meharry Medical College, Nashville, TN 37208.
Gene (NETHERLANDS) May 14 1990, 89 (2) p279-82, ISSN 0378-1119 Journal Code: FOP
Contract/Grant No.: HL01989, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
With the goal of using adeno-associated viruses (AAV) as the gene-transfer vector for gene therapy of hemoglobinopathies, human beta-globin cDNA was ligated downstream from the P40 promoter of the AAV type-2 (AAV2) genome. To circumvent difficulties of cloning DNA containing palindromic sequences, two of which exist in the termini of AAV genome, a step-wise approach handling one palindrome at a time was devised to construct the chimeric expression vector. Electroporation of the construct into human 293 cells (embryonal kidney cell line) resulted in expression of the cloned human beta-globin cDNA, as evidenced by the synthesis of transcripts hybridizable to human beta-globin cDNA probe. Addition of the 3'-end region of AAV DNA that contains both the transcription termination signal and origin of DNA replication for AAV to the construct permitted the recombinant AAV genome to be rescued and replicate in the cell.

9/7/18
DIALOG(R)File 155:MEDLINE(R)
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06306491 88322865
Expression and rescue of a nonselected marker from an integrated AAV vector.
Mendelson E; Smith MG; Carter BJ
Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive, and Kidney Diseases, Bethesda, Maryland 20892.
Virology (UNITED STATES) Sep 1988, 166 (1) p154-65, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We used rep+ and rep- recombinant AAV-plasmid vectors containing the nonselectable marker chloramphenicol acetyltransferase (CAT) driven by the AAV p40 promoter, and having a selectable marker, neo, inserted in the plasmid genome, and driven by a herpesvirus thymidine kinase gene promoter. Each vector was transfected into human 293 cells or HeLa cells and the neo gene was used to select geneticin-resistant (genr) cells containing integrated vectors. The genr cells were then screened for expression of the unselected marker CAT. For 293 cells, most clones from the rep- vector gave high CAT expression whereas only 50% of those from the rep+ vector expressed CAT, generally at low level. For HeLa cells about 25% of the clones derived from either the rep+ or rep- vector expressed CAT, and several clones from the rep+ vector gave very high yields. We also analyzed integrated rep+ vectors by rescue after superinfection with adenovirus and by Southern blotting. The AAV-CAT genome could be rescued from 50% of HeLa cell clones but not from 293 cell clones. Lack of rescuability reflected rearrangement of the AAV genome termini or the rep gene. Western blotting showed low level constitutive expression of rep protein in one 293 cell clone and two HeLa cell clones. Thus, the AAV p40 promoter (as well as p5 and p19) can function in integrated vectors to express unselected markers which can subsequently be rescued. Expression and rescue depended upon several parameters including the cell type, the initial structure of the vector (rep+ or rep-) but not continued expression of rep, and possibly global effects of the surrounding chromatin.

9/7/21
DIALOG(R)File 155:MEDLINE(R)

06265856 86310795
Adeno-associated virus vector for high-frequency integration, expression, and rescue of genes in mammalian cells.
Tratschin JD; Miller IL; Smith MG; Carter BJ
Mol Cell Biol (UNITED STATES) Nov 1985, 5 (11) p3251-60, ISSN 0270-7306 Journal Code: NGY
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We describe the construction of an adeno-associated virus (AAV) vector in which the coding sequence of the procaryotic gene neo is expressed under the control of the major AAV promoter p40. This AAV-neo vector allowed stable expression of neo as a dominant selective marker in mammalian cells by selection of cells which were resistant to the antibiotic geneticin (G418). When the vector was introduced into human (293 or HeLa) cell lines by a DNA transfection procedure, stable geneticin-resistant colonies were obtained. When the vector was first packaged into AAV particles and then introduced into cells via particle infection, geneticin-resistant cells were obtained at higher frequencies than those obtained by DNA transfection. In geneticin-resistant cells the AAV-neo vector was integrated at low copy number and could be rescued by subsequent infection with wild-type AAV and the helper adenovirus or, in some cases, by infection with adenovirus alone. The rescued AAV-neo vector could then be recovered as amplified unintegrated DNA from a Hirt lysate. These results demonstrate that AAV can be used as a transducing viral vector for stable integration and expression of a foreign gene in mammalian cells. The high frequency of integration and the ability to rescue the integrated vector suggest that this vector system may be useful for selecting genes from cDNA libraries. This vector may also be useful for introduction of genes into cells which are refractory to transfection in procedures such as those involving the use of CaPO4 or DEAE-dextran.

9/7/26
DIALOG(R)File 155:MEDLINE(R)

06133420 87321122
Gene expression in adeno-associated virus vectors: the effects of chimeric mRNA structure, helper virus, and adenovirus VA1 RNA.
West MH; Trempe JP; Tratschin JD; Carter BJ
Virology (UNITED STATES) Sep 1987, 160 (1) p38-47, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We used a recombinant plasmid containing an adeno-associated virus (AAV) genome to construct several vectors which express the gene for chloramphenicol acetyltransferase (CAT). We transfected four different AAV-CAT vectors into human 293 (adenovirus-transformed) cells and analyzed CAT activity. We show that, for vectors using the AAV p40 and p19 promoter, the chimeric AAV-CAT transcripts began from the correct 5' position but the basal level of CAT expression depended in part on the structure of the transcript. We also examined the effects of coinfection of the cells with the helper adenovirus or cotransfection with a plasmid which expressed the adenovirus translational control RNA, VA1 RNA. Cotransfection with plasmids containing the gene for VA1 RNA resulted in elevated levels of CAT activity. VA1 RNA stimulated translation of the chimeric mRNA. However, in two cases, the VA1 RNA apparently decreased the level of mRNA. These results suggest that in addition to its function in translation, VA1 RNA acts at a second site to alter cytoplasmic accumulation of some mRNAs.

Infection with adenovirus increased CAT activity several-fold by increasing the cytoplasmic levels of the chimeric AAV-CAT transcript. When the CAT gene is inserted down stream of the AAV intron, adenovirus and not VA1 RNA alone increased CAT activity by promoting accumulation of a spliced transcript.

9/7/31
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
05368677 88288213
Cloning of the human thyrotropin beta-subunit gene and transient expression of biologically active human thyrotropin after gene transfection.
Wondisford FE; Usala SJ; DeCherney GS; Castren M; Radovick S; Gyves PW; Trempe JP; Kerfoot BP; Nikodem VM; Carter BJ; et al
Molecular, Cellular and Nutritional Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland 20892.
Mol Endocrinol (UNITED STATES) Jan 1988, 2 (1) p32-9, ISSN 0888-8809 Journal Code: NGZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A 17 kilobase pair fragment of DNA containing the human TSH (hTSH) beta-subunit gene was isolated from a human leukocyte genomic library. Using a 621 base pair human CG alpha-subunit cDNA and a 2.0 kilobase pair genomic fragment of hTSH beta containing both coding exons, we constructed hCG alpha and hTSH beta expression vectors containing either the early promoter of simian virus 40 or the promoters of adeno-associated virus. Cotransfection of two adeno-associated virus vectors, each containing one subunit of hTSH, together with a plasmid containing the adenovirus VA RNA genes produced hTSH as well as free human alpha- and TSH beta-subunits in an adenovirus transformed human embryonal kidney cell line (293). The levels of protein expression in this system were 10- to 100-fold greater than that found in a simian virus transformed monkey kidney cell line (COS) using vectors containing the early promoter of simian virus 40. The hTSH synthesized in 293 cells was glycosylated as indicated by complete binding to concanavalin A-Sepharose but was larger in apparent molecular weight than a standard hTSH preparation on gel chromatography suggesting an altered glycosylation pattern. However, it was immunologically and biologically indistinguishable from two pituitary hTSH standards in an immunoradiometric and in vitro iodide trapping assay, respectively.
? s expression(1a)control?
S10 0 EXPRESSION(1A)CONTROL?
? s express?(2n)control?
463257 EXPRESS?
1188330 CONTROL?
S11 7846 EXPRESS?(2N)CONTROL?
? ds

Set Items Description
S1 2337031 PY=1993:1999
S2 761 AAV OR ADENO(W)ASSOCIATED
S3 770 S2 OR ADENOASSOCIATED
S4 867589 SPECIFIC?
S5 222 S3 AND S4
S6 73 S5 NOT S1
S7 63088 PROMOTER OR PROMOTERS
S8 49 S3 AND S7 NOT S1
S9 33 S8 NOT S6
S10 0 EXPRESSION(1A)CONTROL?
S11 7846 EXPRESS?(2N)CONTROL?
? s s11 and s2 not (s1 or s6 or s9)
7846 S11
761 S2
2337031 S1
73 S6
33 S9
S12 0 S11 AND S2 NOT (S1 OR S6 OR S9)
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$11.31 Estimated cost File155
FTSNET 0.266 Hrs.
$11.31 Estimated cost this search
$11.50 Estimated total session cost 2.695 DialUnits

File 357:Derwent Biotechnology Abs 1982-1999/Feb B2
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See HELP NEWS 357 for details.

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Set    Items  Description
S1     84703  PY=1993:1999
S2       504  AAV OR ADENO(W)ASSOCIATED
S3       504  S2 OR ADENOASSOCIATED
S4     44778  SPECIFIC?
S5       140  S3 AND S4
S6         5  S5 NOT S1
S7     17783  PROMOTER OR PROMOTERS
S8        16  S3 AND S7 NOT S1
S9        16  S8 NOT S6
S10        0  EXPRESSION(1A)CONTROL?
S11     2028  EXPRESS?(2N)CONTROL?
S12        0  S11 AND S2 NOT (S1 OR S6 OR S9)
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6/7/1

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0144085 DBA Accession No.: 93-02137
Status of ribozyme and antisense-based developmental approaches for anti-HIV-1 therapy - adeno-associated virus vector for antisense DNA and antisense RNA expression for HIV virus-1 gene therapy (conference paper)
AUTHOR: Zaia J A; Chatterjee S; Wong K K; Elkins D; Taylor N R; Rossi J J
CORPORATE SOURCE: Division of Pediatrics, City of Hope National Medical Center, Duarte, California 91010-0269, USA.
JOURNAL: Ann.N.Y.Acad.Sci. (660, 95-106) 1992
CODEN: ANYAA9
LANGUAGE: English
ABSTRACT: The adeno-associated virus (AAV) may be a candidate vector for use in virucide gene therapy. Antisense DNA and RNA have been shown to inhibit HIV virus-1 as either synthetic DNA or expressed RNA (intracellular immunization). Systems are being developed for inserting into the host cell genome the DNA sequences that could potentially confer resistance to HIV virus replication. A modified vector system based on the nonpathogenic, replication-defective parvo virus AAV. AAV directs the stable integration of foreign DNA encoding an HIV virus-1-specific antisense RNA. The target for the antisense RNA-transcript is the TAR sequence (a cis-acting RNA stem-loop structure in the HIV virus-1 long terminal repeat). The targeted region, TAR, is highly conserved between HIV virus-1 and SIV virus. Antisense-expressing clonal cell lines were tested for their ability to restrict both HIV virus-1 and SIV replication. Both HIV virus-1 and SIV production were inhibited in the antisense clones, SIV to a lesser degree than HIV virus-1. There was 85% inhibition of SIV replication in clone IIC4 and 92% inhibition of HIV on day 3 postransfection. (69 ref)

6/7/2

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0138156 DBA Accession No.: 92-10648
Development of recombinant adeno-associated viruses that harbor human beta-globin cDNA/gene towards gene therapy of hemoglobinopathies - adeno-associated virus vector plasmid pAV-delta-KhbG construction and expression in 293, KB and K562 cell culture (conference abstract)
AUTHOR: Ohi S; Webb M S; Sitaric S
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: Miami Short Rep. (1, 116) 1991
CODEN: 9999Y
LANGUAGE: English
ABSTRACT: Recombinant adeno-associated virus-2 (AAV2) vectors harboring human beta-globin (hbG) cDNA were constructed. Chimeric plasmid pAVhbG-psi-1 was constructed as previously described. Plasmid pAV-delta-KhbG was constructed by inserting a full-length hbG cDNA into pAV2-delta-K. The recombinant virus was produced by transfecting the chimeric plasmid into 293 cells together with plasmid pAV2 and AAV2, and preparing the cell lysate at 48 hr post-infection. Upon transfection into 293 cells, the recombinant AAV2 DNA harboring hbG cDNA was rescued from the plasmid and replicated in the cells. This in turn resulted in the production of infectious recombinant AAV. AVhbG-psi-1 expressed mRNA in the virus-infected 293, KB and K562 cells. The second recombinant virus, AV-delta-KhbG expressed hbG protein in the infected 293 cells. To make the expression of hbG cDNA/gene specific to erythroid cells, the erythroid-specific 5'-enhancer elements, DCR/LAR, were spliced into the genome of the recombinant virus. (3 ref)

6/7/3

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0134768 DBA Accession No.: 92-07260
Gene transfer in human lymphocytes using a vector based on adeno-associated virus - B-lymphocyte, T-lymphocyte transformation using AAV/neo vector, which may be useful in gene therapy
AUTHOR: Muro-Cacho C A; Samulski R J; +Kaplan D
CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, 2085 Adelbert Road, Cleveland, OH 44106, USA.
JOURNAL: J.Immunother. (11, 4, 231-37) 1992

CODEN: 5592H
LANGUAGE: English
ABSTRACT: The inverted terminal repeats of adeno-associated virus (AAV), which mediate integration at a specific site in human chromosome-19, were used to establish a vector for gene transfer into human lymphocytes. Epstein-Barr virus-transformed B-lymphocyte JY cells were infected with vector AAV/neo containing the neomycin-resistance gene and AAV inverted terminal repeats in place of the AAV coding region. A neomycin-resistant cell was isolated after 4 wk in the presence of G418. Non-transformed T-lymphocyte CAN.1 was infected with AAV/neo during cloning. While uninfected CAJ0-10 cells (control) showed a marked reduction in proliferative activity in the presence of G418, transformed CAN.1 was not affected. There were no detectable alterations in the functional properties of CAN.1. Rescue and replication of wild-type AAV occurred with AAV super-infection. However, the vector was not rescued and did not replicate, indicating the stability of the integrated vector and demonstrating an additional level of safety incorporated in its construction. An AAV vector may be a viable alternative to retro viruses for gene therapy in lymphocytes. (32 ref)

6/7/5
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0086365 DBA Accession No.: 89-04356 PATENT
Stable and viable recombinant animal cell virus vector construction - by contacting Cre with a virus vector containing a lox site and circular DNA containing a lox site
PATENT ASSIGNEE: Du-Pont 1989
PATENT NUMBER: EP 300422 PATENT DATE: 890125 WPI ACCESSION NO.: 89-025608
(8904)
PRIORITY APPLIC. NO.: US 77145 APPLIC. DATE: 870721
NATIONAL APPLIC. NO.: EP 88111596 APPLIC. DATE: 880719
LANGUAGE: English
ABSTRACT: A method for preparing a stable and viable recombinant virus vector for animal cells by site-specific insertion of a DNA fragment into a virus vector comprises: (1) contacting Cre with a 1st lox site, which has been introduced into the DNA of the animal cell virus vector; and (2) contacting Cre with a 2nd lox site in a separate DNA molecule, which is circular so that Cre effects recombination of the circular DNA with the virus vector DNA at the 1st lox site. The initial virus vector preferably contains a selectable marker gene. The DNA fragment preferably lacks the selectable marker. The 1st lox site is introduced into a nonessential region of the vector, e.g. the gIII gene of pseudorabies virus. The DNA fragment preferably encodes a structural protein, an enzyme, a regulatory molecule, or a fragment of any of these. Each of the lox sites is preferably a loxP or a loxC2 site and the vector is preferably SV40, pseudorabies virus, polyoma virus, an adeno virus, an adeno-associated virus, herpes virus, vaccinia virus, cattle papilloma virus, Epstein-Barr virus, a baculo virus or a retro virus, especially RPV42. (19pp)
? ds

Set Items Description
S1 84703 PY=1993:1999
S2 504 AAV OR ADENO(W)ASSOCIATED
S3 504 S2 OR ADENOASSOCIATED
S4 44778 SPECIFIC?
S5 140 S3 AND S4
S6 5 S5 NOT S1
S7 17783 PROMOTER OR PROMOTERS
S8 16 S3 AND S7 NOT S1
S9 16 S8 NOT S6
S10 0 EXPRESSION(1A)CONTROL?
S11 2028 EXPRESS?(2N)CONTROL?
S12 0 S11 AND S2 NOT (S1 OR S6 OR S9)
? t s9/7/1 3-7 9 10

9/7/1
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0140400 DBA Accession No.: 92-12892 PATENT
New adeno-associated virus-2 hybrid gene vector - for foreign gene integration and DNA rescue in mammal cell culture using a helper virus, e.g. plasmid ins 96/lambda-M
PATENT ASSIGNEE: Univ.Florida-Res.Found. 1992
PATENT NUMBER: US 5139941 PATENT DATE: 920818 WPI ACCESSION NO.: 92-299352 (9236)
PRIORITY APPLIC. NO.: US 785224 APPLIC. DATE: 911025
NATIONAL APPLIC. NO.: US 785224 APPLIC. DATE: 911025
LANGUAGE: English
ABSTRACT: A new hybrid gene vector (capable of transduction of foreign DNA into a mammal cell in the presence of a promoter other than an adeno-associated virus (AAV) transcription promoter) comprises foreign DNA ligated into an AAV-2 genome, in place of or in addition to the cap, lip or rep coding sequence or an AAV sequence excluding the 1st and last 145 bp. The AAV genome is cloned in a prokaryotic or yeast plasmid or phage vector (e.g. plasmid pBR322), and may be the entire AAV DNA or a deletion mutant (e.g. dl52-91 or dl3-94), capable of replication on infection of the mammal cell when complemented in trans by an AAV gene. Methods of transducing foreign DNA into mammal cells by infection of cells with the vector, and methods of rescuing foreign DNA from transduced cells by infection with a helper virus (e.g. plasmid

ins 96/lambda-M) containing genes for replication of the AAV genome or production of AAV, are also new. The vector may be used for reliable insertion of foreign DNA into mammal cells, so that the transferred genetic material is stable with respect to the insertion locus, and which is susceptible to expression and rescue. (12pp)

9/7/3
DIALOG(R)File 357:Derwent Biotechnology Abs

0128750 DBA Accession No.: 92-01242
Construction and expression of a recombinant adeno-associated virus that harbors a human beta-globin-encoding cDNA - potential use in gene therapy of thalassemia or sickle cell anemia; gene cloning in KB, K562 and 293 cell culture; vector construction
AUTHOR: Dixit M; Webb M S; Smart W C; +Ohi S
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, 1005 D.B. Todd Jr. Blvd., Nashville, TN 37208, USA.
JOURNAL: Gene (104, 2, 253-57) 1991
CODEN: GENED6
LANGUAGE: English
ABSTRACT: With the goal of using recombinant adeno-associated virus (AAV) for gene therapy of hemoglobinopathies, plasmid pAVh-beta-G-psi-1 was constructed previously, with a human beta-globin cDNA (HBB) gene downstream from the P40 promoter of AAV-2 DNA. Transfection of a 293 cell culture with the plasmid resulted in expression of HBB at the mRNA level, and rescue and replication of the recombinant AAV genome. The replicated recombinant DNA was packaged into an intact virion by trans-complementation with plasmid pAV2 or defective helper plasmids (plasmid pAV-delta-Bam or plasmid pAVXB). The recombinant virus could be isolated by equilibrium cesium chloride density gradient centrifugation, at a density of 1.4 g/cu cm. The defective helpers were used to produce wild-type AAV-free recombinant AAV. The recombinant AAV was infectious, and produced chimeric mRNA containing the HBB sequence in virus-infected 293, KB (oral epidermoid carcinoma) and K562 (human erythroleukemia) cells. These results may be useful in designing strategies for gene therapy of thalassemia or sickle cell anemia. (29 ref)

9/7/4
DIALOG(R)File 357:Derwent Biotechnology Abs

0124445 DBA Accession No.: 91-12087 PATENT
New adeno-associated virus-derived eukaryotic vector - containing heterologous DNA for protein expression or especially down-regulation of target e.g. HIV virus-1 or herpes simplex virus-1 gene; intracellular immunization and gene therapy
PATENT ASSIGNEE: Nat.Inst.Health-Bethesda 1991
PATENT NUMBER: US 7527195 PATENT DATE: 910702 WPI ACCESSION NO.: 91-237708 (9132)
PRIORITY APPLIC. NO.: US 527195 APPLIC. DATE: 900523
NATIONAL APPLIC. NO.: US 527195 APPLIC. DATE: 900523
LANGUAGE: English
ABSTRACT: Adeno-associated virus (AAV)-based eukaryotic vectors, and cells transfected with these vectors, are new. The vectors are free of AAV coding sequences and consist of: (a) endogenous cis-active DNA for AAV DNA replication, encapsidation and host cell replication; (b) endogenous AAV polyadenylation signal; (c) a promoter; and (d) a heterologous DNA fragment, operably linked to (b) and (c) and present in the sense or antisense direction. The heterologous DNA fragment can encode a foreign protein or viral component. Specified AAV-based eukaryotic vectors (e.g. CWRSV:HIV-ASN and CWRSV:SN) confer intracellular resistance to HIV virus-1 and herpes simplex virus-1 (HSV-1) infection. The vectors can be used to down-regulate a targeted viral (HIV-1, HSV-1) or cellular (histocompatibility gene involved in graft rejection) gene of known sequence, or for protein expression. In a preferred process, the AAV-based vectors are used to produce an antisense mRNA complementary to a 5'-noncoding region of the primary HIV-1 RNA transcript including the core TAR sequence. The mRNA inhibits HIV-1 replication and infectious particle production. (69pp)

9/7/5
DIALOG(R)File 357:Derwent Biotechnology Abs

0110288 DBA Accession No.: 90-12979
Construction of recombinant adeno-associated virus that harbors human beta-globin cDNA - vector construction for potential application in hemoglobinopathy gene therapy; gene cloning and expression in 293 cell culture (conference abstract)
AUTHOR: Ohi S; Dixit M; Tillery M K; Plonk S G
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: J.Cell.Biochem. (Suppl.14A, D422) 1990
CODEN: JCEBD5
LANGUAGE: English
ABSTRACT: The possibility of developing human recombinant parvo virus vectors containing normal alpha-globin or beta-globin cDNA genes for gene therapy of hemoglobinopathies was investigated. The human beta-globin cDNA was excised from JW102 using S1-nuclease and ligated with adeno-associated virus-2 (AAV2) DNA in plasmid pAV2, downstream of the P40 promoter. Cloning of this construct in Escherichia coli DH5 resulted in isolation of recombinant plasmid pAVHbetaGHP11. Transfection via electroporation into human 293 cell culture resulted in expression of the beta-globin cDNA, as evidenced by biosynthesis of transcripts hybridizing to a human beta-globin cDNA probe. Addition of

the 3'-end region of AAV DNA containing both a transcription termination signal and the replication origin for AAV to plasmid pAVHbetaGHP11 resulted in production of plasmid pAVHbetaGpsi1. Transfection of this construct into 293 cells permitted the recombinant AAV DNA containing the beta-globin cDNA to replicate inside the cell. This, in turn, resulted in production of the infectious recombinant virus. (0 ref)

9/7/6

DIALOG(R)File 357:Derwent Biotechnology Abs
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0110266 DBA Accession No.: 90-12957
Construction and replication of an adeno-associated virus expression vector that contains human beta-globin cDNA - plasmid pAVh-beta-GHP11 and plasmid pAVh-beta-G-psi-1 construction; potential application in gene therapy of e.g. sickle cell anemia or thalassemia
AUTHOR: Ohi S; Dixit M; Tillery M K; Plonk S G
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, 1005 D.B. Todd Jr. Blvd., Nashville, TN 37208, USA.
JOURNAL: Gene (89, 2, 279-82) 1990
CODEN: GENED6
LANGUAGE: English
ABSTRACT: With the goal of using an adeno-associated virus (AAV) as a gene transfer vector for gene therapy of hemoglobinopathies (e.g. sickle cell anemia or thalassemia), human beta-globin cDNA was ligated downstream from the P40 promoter of the AAV-2 genome. To circumvent difficulties of cloning DNA containing palindromic sequences, 2 of which exist in the termini of the AAV genome, a stepwise approach handling 1 palindrome at a time was devised to construct a chimeric expression vector, plasmid pAVh-beta-GHP11. Electroporation of the construct into a human 293 cell culture resulted in expression of the cloned human beta-globin cDNA, as evidenced by the biosynthesis of transcripts hybridizable to a human beta-globin cDNA probe. Addition of the 3'-end region of AAV DNA containing both the transcription termination signal and DNA replication origin for AAV to the construct (to give plasmid pAVh-beta-G-psi-1) permitted the recombinant AAV genome to be rescued and replicate in the cell. (17 ref)

9/7/7

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0106673 DBA Accession No.: 90-09364
Production and expression of recombinant adeno-associated viruses harboring human beta-globin cDNA - adeno-associated virus expression in 293 cell culture; potential gene therapy for hemoglobinopathy diseases (conference abstract)
AUTHOR: Ohi S; Dixit M; Plonk S G
CORPORATE SOURCE: Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: FASEB J. (4, 7, A2288) 1990
CODEN: FAJOEC
LANGUAGE: English
ABSTRACT: 2 Plasmids that harbor human beta-globin (hbG) cDNA downstream of the P40 promoter of adeno-associated virus-2 (AAV2) DNA were constructed with the aim of using recombinant human parvo virus for hemoglobinopathy gene therapy. Plasmid pAVhbetaGpsil contains a partial hbG cDNA derived from JW102, whereas plasmid pAVdeltaKhbG contains a full-length hbG cDNA derived from plasmid pB6-6. Upon transfection, pAVhbetaGpsil expressed chimeric RNAs containing hbG sequences in human 293 cells. Recombinant genomes were rescued from both plasmids and replicated in the cell. This led to the production of infections recombinant AAV. When infected in 293 cells, the virus preparation resulted in efficient expression of hbG mRNAs in the cell. (3 ref)

9/7/9

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1999 Derwent Publ Ltd. All rts. reserv.
0086328 DBA Accession No.: 89-04319
Construction and characterization of recombinant adeno-associated virus genome containing human beta-globin cDNA - gene cloning and expression in human cell culture; potential sickle cell anemia or thalassemia gene therapy (conference abstract)
AUTHOR: Ohi S; Dixit M; Tillery M K
CORPORATE SOURCE: Department of Biochemistry and the Sickle Cell Center, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: J.Cell Biol. (107, 6, Pt.3, 304a) 1988
CODEN: JCLBA3
LANGUAGE: English
ABSTRACT: The human parvo virus, adeno-associated virus, is a useful vector for cloning and expression of foreign genes. With the aim of construction of recombinant human parvo viruses containing either alpha-globin or beta-globin genes for gene therapy of hemoglobinopathies, such as sickle cell anemia and thalassemia, a cDNA sequence for human beta-globin was isolated and inserted downstream of the p40 promoter of adeno-associated virus. The beta-globin cDNA was excised from plasmid JW102 using S1 nuclease. The fragment was treated with Escherichia coli DNA-polymerase-I (EC-2.7.7.7), Klenow fragment and blunt-end ligated to plasmid pBR322, followed by cloning in Escherichia coli HB101. 1 Clone, plasmid pHbetaGS3, was amplified and the intact beta-globin cDNA region was excised on a HindIII-NhiI fragment. The fragment was treated with Bal31 and blunt-end ligated to plasmid pAV2 downstream of the p40 promoter (HindIII site). From plasmid pAV2 a KpnI fragment was deleted (plasmid pAVdeltaKpn) to accommodate the foreign DNA. Expression of beta-globin under the control of p40 promoter was tested in human 293 cell culture and

pluripotent K562 cell culture. (2 ref)

9/7/10
DIALOG(R)File 357:Derwent Biotechnology Abs
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0082125 DBA Accession No.: 89-00116
Expression and rescue of a nonselected marker from an integrated AAV vector - chloramphenicol-acetyltransferase gene cloning in human cell culture using adeno-associated virus vector
AUTHOR: Mendelson E; Smith M G; Carter B J
CORPORATE SOURCE: Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive, and Kidney Diseases, Building 8, Room 304, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Virology (166, 1, 154-65) 1988
CODEN: VIRLAX
LANGUAGE: English
ABSTRACT: Rep+ and rep- adeno-associated virus (AAV) vectors (plasmid pEM15 and plasmid pEM612 respectively) were constructed, containing a chloramphenicol-acetyltransferase (EC-2.3.1.28) (CAT) gene driven by the AAV p40 promoter, and a neo gene, driven by a herpes virus thymidine-kinase (EC-2.7.1.21) gene promoter. The vectors were transfected into a human 293 cell or HeLa cell culture, geneticin-resistant cells were selected, and cells were screened for CAT expression. With 293 cells, most rep- clones showed high CAT expression, but only 50% of rep+ clones expressed CAT, at a low level. With HeLa cells 25% of rep+ and rep- clones expressed CAT, some rep+ clones giving high yields. The rep+ vectors were also analyzed by rescue after superinfection with adeno virus and by Southern blot. AAV-CAT DNA could be rescued from 50% of HeLa cells but not from 293 cells. Non-rescue could be due to rearrangement of AAV termini or the rep gene. Western blot analysis showed low constitutive expression of rep protein in 1 293 cell clone and 2 HeLa cell clones. Thus, the AAV p40 promoter could drive expression of non-selected markers in integrated vectors, which could then be rescued. (26 ref)
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DIALINDEX(R)
(c) 1999 The Dialog Corporation plc
*** DIALINDEX search results display in an abbreviated ***
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>>>You must open a minimum of 2 files
? sf allscience
You have 220 files in your file list.
(To see banners, use SHOW FILES command)
? show files

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6: NTIS_64-1999/Mar W3
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9: Business & Industry(R) Jul_1994-1999/Feb 23
10: AGRICOLA_70-1999/Feb
14: Mechanical Engineering Abs_1973-1999/Feb
15: ABI/INFORM(R)_1971-1999/Feb 22
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18: IAC F&S INDEX(R)_1980-1999/Feb 23
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32: METADEX(R)_1966-1999/Apr B1
33: Aluminium Ind Abs_1968-1999/Feb
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47: Magazine Database(TM)_1959-1999/Feb 23

49: PAIS INT._1976-1998/Oct
50: CAB Abstracts_1972-1999/Jan
51: Food Sci.&Tech.Abs_1969-1999/Feb
52: TSCA Chemical Substances Inventory_1998/May
53: FOODLINE(R): Food Science & Technology_1972-1999/Feb 22
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73: EMBASE_1974-1999/Jan W5
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119: Textile Technol.Dig._1978-1999
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180: Federal Register_1985-1999/Feb 22
185: Zoological Record Online(R)_1978-1999/V135P01
187: F-D-C Reports_1987-1999/Feb W2
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211: IAC Newsearch(TM)_1997-1999/Feb 23
220: CLAIMS(R)/Citation(1790-1946)__1998/Q4
221: CLAIMS(R)/Citation(1947-1970)__1998/Q4
222: CLAIMS(R)/Citation(1971-1997)__1998/Q4
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269: Materials Bus.(TM)_1985-1999/Feb
275: IAC(SM) Computer Database(TM)_1983-1999/Feb 23
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303: Chapman & Hall Chemical Database_1997/Apr
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315: ChemEng & Biotec Abs_1970-1999/Mar
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335: Ceramic Abstracts_1976-1998/Q3
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340: CLAIMS(R)/US Patent_1950-99/Feb 16
342: Derwent Patents Citation Indx_1978-98/9907
344: Chinese Patents ABS_Apr 1985-1999/Jan
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636: IAC Newsletter DB(TM)_1987-1999/Feb 23
637: Journal of Commerce_1986-1999/Feb 22
646: Consumer Reports_1982-1999/Feb
647: CMP Computer Fulltext_1988-1999/Feb W2
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766: FIND(R)/SVP Market Research_1993-1999/Feb
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769: Jupiter Market Research_1999/Feb 16
770: Beverage Marketing Research_1999/Feb
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791: State Tax Today_1991-1999/Feb 23

? b 342
23feb99 09:50:02 User208669 Session D1383.5
$0.16 0.124 DialUnits File411
$0.16 Estimated cost File411
FTSNET 0.033 Hrs.
$0.16 Estimated cost this search
$0.54 Estimated total session cost 0.167 DialUnits

File 342:Derwent Patents Citation Indx 1978-98/9907
(c) 1999 Derwent Info Ltd
*File 342: Effective October 1, DialUnit rates adjusted for unrounding.
See HELP NEWS 342 for details.

Set Items Description
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? help news 342
HELP NEWS 342 September 29, 1998
DERWENT PATENTS CITATION INDEX (DPCI)
As you may be aware, Dialog eliminated the rounding of DialUnits, effective 1 September 1998, in order to provide more equitable pricing for users conducting simple searches that incur a fractional DialUnit. This change in the pricing structure was in response to requests by Dialog customers.
In September, the elimination of DialUnit rounding significantly reduced the overall cost of searching DPCI because Derwent chose not to immediately revise their DialUnit pricing. To bring overall costs back in line with pre-September levels, Derwent has increased DialUnit rates effective 1 October 1998. New DialUnit prices for File 342 are as follows:
Non-Japanese Users $8.57
Japanese Users $9.43
Note that for simple searches that incur only a fractional DialUnit, searches remain considerably cheaper than in August. For more elaborate searches, overall costs are now comparable with pre-September levels and with other hosts.
For customers who require budgeting certainty, Dialog offers an alternative to pay-as-you-go pricing. The "Derwent on Dialog Flat-Fee Program" available from Dialog provides unlimited access to all Derwent files, with your flat monthly fee based on your current usage patterns. Please contact your Dialog sales representative for more details.
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S1 1418301 PY=1993:1999
18 AAV
102 ADENO
15118 ASSOCIATED
76 ADENO(W)ASSOCIATED
S2 80 AAV OR ADENO(W)ASSOCIATED
80 S2
0 ADENOASSOCIATED
S3 80 S2 OR ADENOASSOCIATED
S4 21150 SPECIFIC?
80 S3
21150 S4
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8 S5
1418301 S1
S6 0 S5 NOT S1
2923 PROMOTER
606 PROMOTERS
S7 3509 PROMOTER OR PROMOTERS
80 S3
3509 S7
1418301 S1
S8 0 S3 AND S7 NOT S1
0 S8
0 S6
S9 0 S8 NOT S6
S10 0 EXPRESSION(1A)CONTROL?
4848 EXPRESS?
296089 CONTROL?
S11 143 EXPRESS?(2N)CONTROL?
143 S11
80 S2
1418301 S1
0 S6
0 S9
S12 0 S11 AND S2 NOT (S1 OR S6 OR S9)
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2/7/1
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03298330 WPI Acc No: 98-557524/47
New vector containing therapeutic gene inserted between adeno-associated virus inverted terminal repeats - useful as safe gene therapy vectors

providing site-specific integration
Patent Assignee: (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI
Author (Inventor): CILIBERTO G; COLLOCA S; FATTORI E; FIPALDINI C; LA MONICA N; MONCIOTTI A; PALOMBO F; PIERONI L; RECCHIA A; RIZZUTO G
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9845462 A1 981015 (BASIC)
AU 9870778 A 981030
Derwent Week (Basic): 9847
Priority Data: IT 97RM0200 (970408)
Applications: AU 9870778 (980408); WO 98IT82 (980408)
Designated States
(National): AU; CA; CN; IL; JP; KR; MX; US
(Regional): AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
Derwent Class: B04; D16
Int Pat Class: A61K-048/00; C12N-005/12
Number of Patents: 002
Number of Countries: 026
Number of Cited Patents: 004
Number of Cited Literature References: 005
Number of Citing Patents: 000

2/7/2
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03226721 WPI Acc No: 98-495836/42
Separating viruses of different sizes by filtration - particularly recovery of recombinant adeno-associated virus particles for gene therapy from infectious adenovirus(es)
Patent Assignee: (MEDI-) MEDIGENE AG
Author (Inventor): BOGEDAIN C; MAASS G; HOERER M
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9839420 A1 980911 (BASIC)
DE 19709186 A1 980917 C12N-001/2; C12N-007/2
Derwent Week (Basic): 9842
Priority Data: DE 1009186 (970306)
Applications: DE 1009186 (970306); WO 98EP1257 (980305)
Designated States
(National): AU; CA; JP; US
(Regional): AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
Derwent Class: A96; B04; D16
Int Pat Class: A61K-048/00; C12N-001/02; C12N-007/02
Number of Patents: 002
Number of Countries: 021
Number of Cited Patents: 007
Number of Cited Literature References: 003
Number of Citing Patents: 000

2/7/3
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03214195 WPI Acc No: 98-333055/29
Expression of polynucleotide(s) in mammals - by administering viral particles comprising recombinant adeno-associated virus to liver cells, used for, e.g. treating liver tumours
Patent Assignee: (SOMA-) SOMATIX THERAPY CORP; (UNIW) UNIV WASHINGTON
Author (Inventor): SNYDER R; DANOS O; COHEN L; KAY M; THOMPSON A R
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9824479 A1 980611 (BASIC)
AU 9855882 A 980629
Derwent Week (Basic): 9829
Priority Data: US 32506 (961202); US 882044 (970625)
Applications: WO 97US21398 (971202); AU 9855882 (971202)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU ; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A61K-048/00; C12N-007/01; C12N-015/10; C12N-015/63; C12N-015/86; C12Q-001/68
Number of Patents: 002
Number of Countries: 079
Number of Cited Patents: 001
Number of Cited Literature References: 002
Number of Citing Patents: 000

2/7/4
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03213179 WPI Acc No: 98-297948/26
Hybrid gene vector containing herpes and adeno-associated components - plus trans-gene for delivery to mitotic or non-mitotic cells, useful in gene therapy, provides stable expression and can accommodate large trans-genes
Patent Assignee: (GEHO) GEN HOSPITAL CORP; (SHRI-) SHRIVER CENT MENTAL

RETARDATION EUNICE
Author (Inventor): BREAKEFIELD X O; JACOBY D R; SMITH F I
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9821345 A1 980522 (BASIC)
AU 9851999 A 980603
Derwent Week (Basic): 9826
Priority Data: US 747919 (961112)
Applications: WO 97US20422 (971112); AU 9851999 (971112)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; UZ; VN; YU; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A01N-043/04; A61K-031/70
Number of Patents: 002
Number of Countries: 078
Number of Cited Patents: 000
Number of Cited Literature References: 003
Number of Citing Patents: 000

2/7/5
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03192851 WPI Acc No: 98-230428/20
New methods for gene therapy - by administering subcutaneously or topically a recombinant adeno-associated virus vector which expresses a gene of interest
Patent Assignee: (CELL-) CELL GENESYS INC
Author (Inventor): SNYDER R; DANOS O; MCARTHUR J; MULLIGAN R
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9813070 A1 980402 (BASIC)
AU 9747367 A 980417
Derwent Week (Basic): 9820
Priority Data: US 26638 (960925)
Applications: AU 9747367 (970925); WO 97US16929 (970925)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU ; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A61K-009/08; A61K-048/00
Number of Patents: 002
Number of Countries: 079
Number of Cited Patents: 002
Number of Cited Literature References: 002
Number of Citing Patents: 000

2/7/6
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03191639 WPI Acc No: 98-193255/17
Novel adeno-associated viral vectors - for liver specific delivery of therapeutic molecule
Patent Assignee: (CHIR) CHIRON CORP; (INDV) UNIV INDIANA
Author (Inventor): SRIVASTAVA A; PONNAZHAGAN S; CHLOEMER R H; WANG X; YODER M C; ZHOU S; ESCOBEDO J; DWARKI V
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9809524 A1 980312 (BASIC)
Derwent Week (Basic): 9817
Priority Data: US 25616 (960906); US 25649 (960911)
Applications: WO 97US15453 (970902)
Designated States
(National): CA; JP
(Regional): AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
Derwent Class: B04; D16
Int Pat Class: A01N-043/04; A61K-031/70
Number of Patents: 001
Number of Countries: 019
Number of Cited Patents: 001
Number of Cited Literature References: 007
Number of Citing Patents: 000

2/7/7
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03182693 WPI Acc No: 98-377242/32
Transfection of primate pluripotent haematopoietic stem cells with an adeno-associated viral vector - useful for expressing e.g. a therapeutic protein in pluripotent cells for the treatment of diseases such as sickle cell anaemia
Patent Assignee: (INTR-) INTROGENE BV
Author (Inventor): EINERHAND M P W; VALERIO D

Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9824924 A1 980611 (BASIC)
Derwent Week (Basic): 9832
Priority Data: EP 96203444 (961205)
Applications: WO 97NL631 (971119)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU ; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A61K-048/00; C12N-005/10
Number of Patents: 001
Number of Countries: 079
Number of Cited Patents: 003
Number of Cited Literature References: 003
Number of Citing Patents: 000

2/7/8
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03182343 WPI Acc No: 98-362776/31
Polynucleotide comprising adeno-associated virus, useful for gene therapy - comprise an AAV packaging site containing promoter and site-specific recombination sequences for activation by recombinase
Patent Assignee: (TARG-) TARGETED GENETICS CORP
Author (Inventor): BURSTEIN H
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9827207 A1 980625 (BASIC)
Derwent Week (Basic): 9831
Priority Data: US 41689 (961218)
Applications: WO 97US23018 (971212)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; GW; HU; ID; IL; IS; JP; KE; KG; KP ; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ ; VN; YU; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: C07K-014/015; C07K-014/47; C12N-005/10; C12N-007/01; C12N-009/00; C12N-015/12; C12N-015/85
Number of Patents: 001
Number of Countries: 081
Number of Cited Patents: 003
Number of Cited Literature References: 005
Number of Citing Patents: 000

2/7/9
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03182340 WPI Acc No: 98-362773/31
High efficiency packaging of recombinant adeno-associated virus vector - containing at least one AAV split-cap, AAV rep78 or AAV rep52 split-packaging gene, used for transfecting mammalian cells
Patent Assignee: (TARG-) TARGETED GENETICS CORP
Author (Inventor): ALLEN J M; STEPAN A M; QUINTON T J; LUPTON S D
Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9827204 A2 980625 (BASIC)
Derwent Week (Basic): 9831
Priority Data: US 41609 (961218)
Applications: WO 97US23247 (971212)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HU; ID; IL; IS; JP; KE; KG; KP; KR ; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN ; YU; ZW
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: C12N-015/00
Number of Patents: 001
Number of Countries: 080
Number of Cited Patents: 004
Number of Cited Literature References: 001
Number of Citing Patents: 000

2/7/10
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 1999 Derwent Info Ltd. All rts. reserv.
03162607 WPI Acc No: 97-099896/09
Expressing gene prod. in muscle using adeno-associated viral vector - providing efficient, long-term expression and able to infect non-dividing cells
Patent Assignee: (UYNC-) UNIV NORTH CAROLINA
Author (Inventor): XIAO X; SAMULSKI R J

Patent Family:
Patent No Kind Date Examiner Field of Search
WO 9640272 A1 961219 (BASIC)
AU 9662686 A 961230
EP 844887 A1 980603
Derwent Week (Basic): 9709
Priority Data: US 487005 (950607)
Applications: AU 9662686 (960605); EP 96921468 (960605); WO 96US9879 (960605)
Designated States
(National): AU; CA; IL; JP
(Regional): AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
Derwent Class: B04; D16
Int Pat Class: A61K-048/00
Number of Patents: 003
Number of Countries: 022
Number of Cited Patents: 000
Number of Cited Literature References: 001
Number of Citing Patents: 001
CITING PATENTS
Family Member Citing Patent Cat WPI Acc No Assignee/Inventor
By Examiner:
WO 9640272 A1 US 5846528 A 97-385339/35 (AVIG-) AVIGEN INC/
PODSAKOFF G M; KURTZMAN G J
? log hold
23feb99 09:51:48 User208669 Session D1383.6
$7.77 0.856 DialUnits File342
$0.00 20 Type(s) in Format 6
$57.30 10 Type(s) in Format 7
$57.30 30 Types
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$65.61 Estimated total session cost 1.024 DialUnits
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23feb99 09:28:24 User208669 Session D1383.1
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FTSNET 0.002 Hrs.
$0.19 Estimated cost this search
$0.19 Estimated total session cost 0.059 DialUnits

File 155:MEDLINE(R) 1966-1999/Apr W1
(c) format only 1999 Dialog Corporation

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Set Items Description
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S2 761 AAV OR ADENO(W)ASSOCIATED
S3 770 S2 OR ADENOASSOCIATED
S4 867589 SPECIFIC?
S5 222 S3 AND S4
S6 73 S5 NOT S1
S7 63088 PROMOTER OR PROMOTERS
S8 49 S3 AND S7 NOT S1
S9 33 S8 NOT S6
S10 0 EXPRESSION(1A)CONTROL?
S11 7846 EXPRESS?(2N)CONTROL?
? t s6/7/6 8 9 14 18 24 36

6/7/6
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.
07333400 93043547
Adeno-associated virus vectors.
Carter BJ
Targeted Genetics Corporation, Seattle, Washington.
Curr Opin Biotechnol (ENGLAND) Oct 1992, 3 (5) p533-9, ISSN 0958-1669
Journal Code: A92
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Adeno-associated virus is a human parvovirus that integrates its DNA genome into host cell chromosomes with very high efficiency. This suggests that adeno-associated virus may be a useful vector for human gene therapy. Interest in adeno-associated virus vectors increased greatly in the last year following reports that adeno-associated virus genome integration may be site specific and occur at preferred sites in the human genome. Several genes relevant to the treatment of genetic or infectious diseases have been expressed in adeno-associated virus vectors in vitro. (51 Refs.)

Abs is Not provided

6/7/8
DIALOG(R)File 155:MEDLINE(R)
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07296175 92410609
Modulation of the cellular phenotype by integrated adeno-associated virus.
Winocour E; Puzis L; Etkin S; Koch T; Danovitch B; Mendelson E; Shaulian E; Karby S; Lavi S
Department of Molecular Genetics and Virology, Weizmann Institute of Science, Rehovot, Israel.
Virology (UNITED STATES) Sep 1992, 190 (1) p316-29, ISSN 0042-6822
Journal Code: XEA
Contract/Grant No.: AI-26122, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The adeno-associated virus (AAV) rep gene encodes a series of overlapping, multifunctional, nonstructural proteins (Rep proteins) which regulate the viral life cycle and which are also capable of trans-regulating nonviral gene expressions (reviewed in Berns, 1990, Microbiol. Rev. 54, 316-329). To investigate the expression of the AAV rep gene in a cellular chromosomal context, SV40-transformed Chinese hamster embryo (OD4) cells were infected with an AAV/neo hybrid virus and progeny resistant to the antibiotic G418 were selected and amplified. Chromosomal integration and RNA transcription of the AAV and neo DNA inserts were confirmed by Southern and Northern blotting procedures. One of the G418R cell lines stably expressed a protein which reacted specifically with AAV anti-Rep antiserum in Western immunoblots. The stable integration of AAV rep DNA, which did not interfere with cell proliferation under normal growth conditions, was associated with two changes in cellular phenotype: eight of nine lines were markedly more sensitive to UV light (254 nm) than were the parental OD4 cells; and seven of the nine lines had lost the capacity to promote SV40 origin DNA amplification in vitro, in contrast to the parental OD4 cells. OD4 cells transformed to G418R by AAV/neo DNA constructs with a deleted rep gene, or by a neo DNA construct lacking AAV DNA, did not display these phenotypic changes. It is suggested that stable integration of the AAV rep gene interferes with cellular processes connected with DNA repair and gene amplification.

6/7/9
DIALOG(R)File 155:MEDLINE(R)
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07288855 92287906
Gene transfer in human lymphocytes using a vector based on adeno-associated virus.
Muro-Cacho CA; Samulski RJ; Kaplan D

NOS

Institute of Pathology, Case Western Reserve University, Cleveland, Ohio 44106.
J Immunother (UNITED STATES) May 1992, 11 (4) p231-7, ISSN 1053-8550 Journal Code: AZ0
Contract/Grant No.: AI-28923, AI, NIAID; DK-42701, DK, NIDDK; AI-25530, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Adeno-associated virus is a nonpathogenic, dependent parvovirus that integrates at a specific site in human chromosome 19. We have used the inverted terminal repeats of the virus, which mediate integration, to establish a vector for gene transfer in human lymphocytes. A neomycin resistance gene has been stably introduced into nontransformed human T-cell clones and a subsequent analysis of the functional properties of the infected clone revealed no detectable alterations. Rescue and replication of the wild-type virus was accomplished with adenovirus superinfection; however, the vector was not rescued and did not replicate by this procedure, indicating the stability of the integrated vector and demonstrating an additional level of safety incorporated in its construction. An adeno-associated virus-based vector represents an alternative to retroviruses for gene therapy in lymphocytes.

6/7/14

06954089 92037558
Targeted integration of adeno-associated virus (AAV) into human chromosome 19 [published erratum appears in EMBO J 1992 Mar;11(3):1228]
Samulski RJ; Zhu X; Xiao X; Brook JD; Housman DE; Epstein N; Hunter LA
Department of Biological Sciences, University of Pittsburgh, PA 15260.
EMBO J (ENGLAND) Dec 1991, 10 (12) p3941-50, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI 25530-03, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A key feature in adeno-associated virus (AAV) replication is efficient integration of the viral genome into host cell DNA to establish latency when helper virus is absent. The steps involved in this process remain largely uncharacterized, even though AAV integration was first documented 20 years ago. Using a protein--DNA binding method we isolated AAV--cellular junction DNA sequences. The cellular component hybridized to a single restriction fragment in the virus-free parental cell line, and also co-migrated with AAV-specific sequences in numerous latently infected cell lines. Analysis of somatic cell hybrids indicated that this cellular sequence maps to the distal portion of the q arm of human chromosome 19. In situ hybridization of AAV DNA to chromosomes from latently infected cells confirms the physical location of AAV integrations to be q13.4-ter of chromosome 19. Sequence analysis of several independent integration sites shows breakpoints occurring within a 100 bp cellular region. This non-pathogenic parvovirus thus appears to establish viral latency by integrating its DNA specifically into one chromosomal region. Such specific integration is so far unique among the eukaryotic DNA viruses. The incorporation of site-specific integration into AAV vector schemes should make this vector system attractive for human gene therapy approaches.

6/7/18

06829588 92052179
Isolation of a candidate repressor/activator, NF-E1 (YY-1, delta), that binds to the immunoglobulin kappa 3' enhancer and the immunoglobulin heavy-chain mu E1 site.
Park K; Atchison ML
Department of Animal Biology, University of Pennsylvania, School of Veterinary Medicine, Philadelphia 19104.
Proc Natl Acad Sci U S A (UNITED STATES) Nov 1 1991, 88 (21) p9804-8, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: RO1 GM42415, GM, NIGMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have determined that the developmental control of immunoglobulin kappa 3' enhancer (kappa E3') activity is the result of the combined influence of positive- and negative-acting elements. We show that a central core in the kappa E3' enhancer is active at the pre-B-cell stage but is repressed by flanking negative-acting elements. The negative-acting sequences repress enhancer activity in a position- and orientation-independent manner at the pre-B-cell stage. We have isolated a human cDNA clone encoding a zinc finger protein (NF-E1) that binds to the negative-acting segment of the kappa E3' enhancer. This protein also binds to the immunoglobulin heavy-chain enhancer mu E1 site. NF-E1 is encoded by the same gene as the YY-1 protein, which binds to the adeno-associated virus P5 promoter. NF-E1 is also the human homologue of the mouse delta protein, which binds to ribosomal protein gene promoters. The predicted amino acid sequence of this protein contains features characteristic of transcriptional activators as well as transcriptional repressors. Cotransfection studies with this cDNA indicate that it can repress basal promoter activity. The apparent dual function of this protein is discussed.

6/7/24

06626755 90192777
Site-specific integration by adeno-associated virus.
Kotin RM; Siniscalco M; Samulski RJ; Zhu XD; Hunter L; Laughlin CA;

McLaughlin S; Muzyczka N; Rocchi M; Berns KI
Hearst Microbiology Research Center, Department of Microbiology, Cornell University Medical College, New York, NY 10021.
Proc Natl Acad Sci U S A (UNITED STATES) Mar 1990, 87 (6) p2211-5, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: AI22251, AI, NIAID; GM37090, GM, NIGMS; AI25530, AI, NIAID; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Cellular sequences flanking integrated copies of the adeno-associated virus (AAV) genome were isolated from a latently infected clonal human cell line and used to probe genomic blots derived from an additional 21 independently derived clones of human cells latently infected with AAV. In genomic blots of uninfected human cell lines and of primary human tissue, each flanking-sequence probe hybridized to unique bands, but in 15 of the 22 latently infected clones the flanking sequences hybridized not only to the original fragments but also to a total of 36 additional species. AAV probes also hybridized to 22 of these new bands, representing 11 of the 15 positive clones, but never to the fragment characteristic of uninfected cell DNA. From these data we conclude that the AAV genome preferentially integrates into a specific region of the cellular genome. We have determined that the integration site is unique to chromosome 19 by somatic cell hybrid mapping, and this sequence has been isolated from uninfected human DNA.

6/7/36
DIALOG(R)File 155:MEDLINE(R)
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06116071 87036912
Latent infection of KB cells with adeno-associated virus type 2.
Laughlin CA; Cardellichio CB; Coon HC
J Virol (UNITED STATES) Nov 1986, 60 (2) p515-24, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: R01 AI/CA 19934, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Adeno-associated virus (AAV) is a prevalent human virus whose replication requires factors provided by a coinfecting helper virus. AAV can establish latent infections in vitro by integration of the AAV genome into cellular DNA. To study the process of integration as well as the rescue of AAV replication in latently infected cells after superinfection with a helper virus, we established a panel of independently derived latently infected cell clones. KB cells were infected with a high multiplicity of AAV in the absence of helper virus, cloned, and passaged to dilute out input AAV genomes. AAV DNA replication and protein synthesis were rescued from more than 10% of the KB cell clones after superinfection with adenovirus type 5 (Ad5) or herpes simplex virus types 1 or 2. In the absence of helper virus, there was no detectable expression of AAV-specific RNA or proteins in the latently infected cell clones. Ad5 superinfection also resulted in the production of infectious AAV in most cases. All mutant adenoviruses tested that were able to help AAV DNA replication in a coinfection were also able to rescue AAV from the latently infected cells, although one mutant, Ad5hr6, was less efficient at AAV rescue. Analysis of high-molecular-weight cellular DNA indicated that AAV sequences were integrated into the cell genome. The restriction enzyme digestion patterns of the cellular DNA were consistent with colinear integration of the AAV genome, with the viral termini present at the cell-virus junction. In addition, many of the cell lines appeared to contain head-to-tail concatemers of the AAV genome. The understanding of the integration of AAV DNA is increasingly important since AAV-based vectors have many advantages for gene transduction in vitro and in vivo.
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9/7/4
DIALOG(R)File 155:MEDLINE(R)
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07382011 92348451
Chromosomal localization and organization of the murine genes encoding the beta subunits (AIC2A and AIC2B) of the interleukin 3, granulocyte/macrophage colony-stimulating factor, and interleukin 5 receptors.
Gorman DM; Itoh N; Jenkins NA; Gilbert DJ; Copeland NG; Miyajima A
Department of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, California 94304.
J Biol Chem (UNITED STATES) Aug 5 1992, 267 (22) p15842-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: NO1-CO-74101, CO, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Chromosomal genes for two mouse homologous beta subunits (AIC2A and AIC2B) of the interleukin-3, granulocyte/macrophage colony-stimulating factor, and interleukin-5 receptors were characterized. Both AIC2A and AIC2B genes were present on a 250-kilobase MluI restriction fragment and were mapped on murine chromosome 15 (these loci were provisionally designated as Il3rb-1 (AIC2A) and Il3rb-2 (AIC2B)), closely linked to the c-sis locus. Both genes consist of 14 exons and span about 28 kb each. The major transcription initiation sites of both genes were mapped at 194 bp from the initiation codon. These genes are 95% identical up to 700 bp from the transcription initiation sites. Potential recognition sequences for hemopoietic transcription factors including GATA-1 and PU.1 in addition to a TATA-like sequence are present in the 5'-flanking region. A stretch of 20 bp including the initiation site is homologous to the corresponding region of the erythropoietin receptor and the interleukin-7 receptor genes and to the initiator sequence of the adeno-associated virus P5 promoter,

suggesting a possible role in transcription initiation. Comparison of the exon/intron boundaries of AIC2A and AIC2B genes with those of other members of the cytokine receptor superfamily reveals a conserved evolutionary structure. Isolation of various forms of AIC2 cDNAs reveals differential splicing of the transcripts.

9/7/5
DIALOG(R)File 155:MEDLINE(R)

07330679 90329218
The recombinant human parvoviruses for gene therapy of hemoglobinopathies.
Dixit M; Tillery MK; Plonk SG; Ohi S
Department of Biochemistry, Meharry Medical College, Nashville, TN 37208.
SAAS Bull Biochem Biotechnol (UNITED STATES) Jan 1990, 3 p63-8, Journal Code: ALK
Contract/Grant No.: HL01989, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Towards a goal of using adeno-associated viruses (AAV), the human parvovirus, as the gene transfer vector for gene therapy of hemoglobinopathies, the human beta-globin (h beta G) cDNA was ligated downstream of the P40 promoter of AAV type 2 (AAV2) genome. Transfection via electroporation of the construct into human 293 cells (embryonal kidney cell line) resulted in expression of the cloned h beta G cDNA, as evidenced by the synthesis of transcripts hybridizable to h beta G probe. The transfection led to the recombinant genome to be excised out of the plasmid and replicate in the cell, followed by production of the recombinant AAV that harbors h beta G cDNA.

9/7/6
DIALOG(R)File 155:MEDLINE(R)

07302580 93099882
Characterization of a preferred site on human chromosome 19q for integration of adeno-associated virus DNA by non-homologous recombination.
Kotin RM; Linden RM; Berns KI
Molecular Hematology Branch, National Institutes of Health, Bethesda, MD 20892.
EMBO J (ENGLAND) Dec 1992, 11 (13) p5071-8, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI 22251, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The human parvovirus, adeno-associated virus (AAV), has been shown to integrate preferentially into human chromosome 19 q13.3-qter. The human target sequence for AAV integration (AAVS1) was cloned and sequenced. By analysis of the proviral junctions it was determined that integration of the AAV DNA occurred via a non-homologous recombination pathway although there were either four or five identical nucleotides at the junctions. Integration was a multistep, concerted process that resulted in cellular sequence rearrangements. The sequence of the integration locus was analyzed for possible recombination signals. Direct repeats at a much greater than random occurrence were found distributed non-uniformly throughout the AAVS1 sequence. A CpG island containing transcription factor binding site elements is suggestive of a TATA-less promoter. Evidence for transcriptional activity was provided by PCR amplification of reverse transcribed RNA.

9/7/8
DIALOG(R)File 155:MEDLINE(R)

07295326 92392571
Gene expression from adeno-associated virus vectors in airway epithelial cells.
Flotte TR; Solow R; Owens RA; Afione S; Zeitlin PL; Carter BJ
Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.
Am J Respir Cell Mol Biol (UNITED STATES) Sep 1992, 7 (3) p349-56, ISSN 1044-1549 Journal Code: AOB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Lung diseases such as cystic fibrosis (CF) might be treated by gene therapy using viral vectors delivered to the airway. One potential vector is the defective human parvovirus, adeno-associated virus (AAV). We examined the AAV p5 transcription promoter for gene expression in immortalized cell lines derived from the airway (IB3-1) or pancreas (CFPAC-1) of CF patients. AAV vectors expressing the prokaryotic genes cat (pAAVp5cat) or neo (pAAVp5neo) from the p5 promoter were evaluated after introduction into IB3-1 or CFPAC-1 cells by lipofection. In transient assays in both cell lines, the cat gene was expressed 5- to 10-fold more efficiently from the p5 promoter than from a simian virus 40 early gene promoter (pSVcat). IB3-1 cells were transformed stably to geneticin resistance by pAAVp5neo at a 5-fold higher efficiency than by an SVneo vector. The AAV inverted terminal repeat (ITR) region immediately upstream of the p5 promoter appears to have an enhancer effect and the promoter also contains a CREB site which confers a response to forskolin. In IB3-1 cells, expression of the cat gene from a p5 promoter was decreased about 5-fold by deletion of both the upstream ITR and the CREB site. The AAVp5neo vector was also packaged into AAV particles and used to infect IB3-1 cells as a transducing virus. Under these conditions, 60 to 70% of the cells could be stably transformed to geneticin resistance. Thus, AAV transducing vectors appear to be a highly efficient delivery system for stable integration and

expression of genes in cultured airway epithelial cells.

9/7/12
DIALOG(R)File 155:MEDLINE(R)

06952402 92009221
Construction and expression of a recombinant adeno-associated virus that harbors a human beta-globin-encoding cDNA.
Dixit M; Webb MS; Smart WC; Ohi S
Department of Biochemistry, School of Medicine, Meharry Medical College, Nashville, TN.
Gene (NETHERLANDS) Aug 15 1991, 104 (2) p253-7, ISSN 0378-1119 Journal Code: FOP
Contract/Grant No.: HL019898, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Towards a goal of using recombinant adeno-associated viruses (AAV) for the gene therapy of hemoglobinopathies we had previously constructed plasmid pAV h beta G psi 1, which contained a human beta-globin-encoding cDNA (HBB) downstream from the P40 promoter of AAV2 DNA [Ohi et al., Gene 89 (1990) 279-282]. Transfection of the plasmid into human 293 cells (embryonal kidney cell line) resulted in the expression of HBB at the mRNA level as well as rescue and replication of the recombinant AAV genome (Ohi et al., ibid.). The present study demonstrates that the replicated recombinant DNA was packaged into an intact virion by transcomplementation with pAV2 or the defective helpers, pAV delta Bam or pAVXB. The recombinant virus could be isolated by equilibrium CsCl density gradient, the density of which was about 1.4 g/cm3. The defective helpers are used to produce wild-type AAV-free recombinant AAV. The recombinant AAV were infectious and expressed chimeric mRNAs containing the HBB sequence in virus-infected 293, KB (oral epidermoid carcinoma cell line) and K562 (human erythroleukemia cell line) cells. The importance of the infectivity and expression of the recombinant AAV in hematopoietic cells is discussed in the context of gene therapy of hemoglobinopathies.

9/7/16
DIALOG(R)File 155:MEDLINE(R)

06634298 90323629
Construction and replication of an adeno-associated virus expression vector that contains human beta-globin cDNA.
Ohi S; Dixit M; Tillery MK; Plonk SG
Department of Biochemistry, School of Medicine, Meharry Medical College, Nashville, TN 37208.
Gene (NETHERLANDS) May 14 1990, 89 (2) p279-82, ISSN 0378-1119 Journal Code: FOP
Contract/Grant No.: HL01989, HL, NHLBI; HL38737, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
With the goal of using adeno-associated viruses (AAV) as the gene-transfer vector for gene therapy of hemoglobinopathies, human beta-globin cDNA was ligated downstream from the P40 promoter of the AAV type-2 (AAV2) genome. To circumvent difficulties of cloning DNA containing palindromic sequences, two of which exist in the termini of AAV genome, a step-wise approach handling one palindrome at a time was devised to construct the chimeric expression vector. Electroporation of the construct into human 293 cells (embryonal kidney cell line) resulted in expression of the cloned human beta-globin cDNA, as evidenced by the synthesis of transcripts hybridizable to human beta-globin cDNA probe. Addition of the 3'-end region of AAV DNA that contains both the transcription termination signal and origin of DNA replication for AAV to the construct permitted the recombinant AAV genome to be rescued and replicate in the cell.

9/7/18
DIALOG(R)File 155:MEDLINE(R)

06306491 88322865
Expression and rescue of a nonselected marker from an integrated AAV vector.
Mendelson E; Smith MG; Carter BJ
Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive, and Kidney Diseases, Bethesda, Maryland 20892.
Virology (UNITED STATES) Sep 1988, 166 (1) p154-65, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We used rep+ and rep- recombinant AAV-plasmid vectors containing the nonselectable marker chloramphenicol acetyltransferase (CAT) driven by the AAV p40 promoter, and having a selectable marker, neo, inserted in the plasmid genome, and driven by a herpesvirus thymidine kinase gene promoter. Each vector was transfected into human 293 cells or HeLa cells and the neo gene was used to select geneticin-resistant (genr) cells containing integrated vectors. The genr cells were then screened for expression of the unselected marker CAT. For 293 cells, most clones from the rep- vector gave high CAT expression whereas only 50% of those from the rep+ vector expressed CAT, generally at low level. For HeLa cells about 25% of the clones derived from either the rep+ or rep- vector expressed CAT, and several clones from the rep+ vector gave very high yields. We also analyzed integrated rep+ vectors by rescue after superinfection with adenovirus and by Southern blotting. The AAV-CAT genome could be rescued from 50% of HeLa cell clones but not from 293 cell clones. Lack of rescuability reflected rearrangement of the AAV genome termini or the rep gene. Western blotting showed low level constitutive expression of rep protein in one 293 cell clone and two HeLa cell clones. Thus, the AAV p40 promoter (as well as p5

and p19) can function in integrated vectors to express unselected markers which can subsequently be rescued. Expression and rescue depended upon several parameters including the cell type, the initial structure of the vector (rep+ or rep-) but not continued expression of rep, and possibly global effects of the surrounding chromatin.

9/7/21
DIALOG(R)File 155:MEDLINE(R)

06265856 86310795
Adeno-associated virus vector for high-frequency integration, expression, and rescue of genes in mammalian cells.
Tratschin JD; Miller IL; Smith MG; Carter BJ
Mol Cell Biol (UNITED STATES) Nov 1985, 5 (11) p3251-60, ISSN 0270-7306 Journal Code: NGY
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We describe the construction of an adeno-associated virus (AAV) vector in which the coding sequence of the procaryotic gene neo is expressed under the control of the major AAV promoter p40. This AAV-neo vector allowed stable expression of neo as a dominant selective marker in mammalian cells by selection of cells which were resistant to the antibiotic geneticin (G418). When the vector was introduced into human (293 or HeLa) cell lines by a DNA transfection procedure, stable geneticin-resistant colonies were obtained. When the vector was first packaged into AAV particles and then introduced into cells via particle infection, geneticin-resistant cells were obtained at higher frequencies than those obtained by DNA transfection. In geneticin-resistant cells the AAV-neo vector was integrated at low copy number and could be rescued by subsequent infection with wild-type AAV and the helper adenovirus or, in some cases, by infection with adenovirus alone. The rescued AAV-neo vector could then be recovered as amplified unintegrated DNA from a Hirt lysate. These results demonstrate that AAV can be used as a transducing viral vector for stable integration and expression of a foreign gene in mammalian cells. The high frequency of integration and the ability to rescue the integrated vector suggest that this vector system may be useful for selecting genes from cDNA libraries. This vector may also be useful for introduction of genes into cells which are refractory to transfection in procedures such as those involving the use of CaPO4 or DEAE-dextran.

9/7/26
DIALOG(R)File 155:MEDLINE(R)

06133420 87321122
Gene expression in adeno-associated virus vectors: the effects of chimeric mRNA structure, helper virus, and adenovirus VA1 RNA.
West MH; Trempe JP; Tratschin JD; Carter BJ
Virology (UNITED STATES) Sep 1987, 160 (1) p38-47, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We used a recombinant plasmid containing an adeno-associated virus (AAV) genome to construct several vectors which express the gene for chloramphenicol acetyltransferase (CAT). We transfected four different AAV-CAT vectors into human 293 (adenovirus-transformed) cells and analyzed CAT activity. We show that, for vectors using the AAV p40 and p19 promoter, the chimeric AAV-CAT transcripts began from the correct 5' position but the basal level of CAT expression depended in part on the structure of the transcript. We also examined the effects of coinfection of the cells with the helper adenovirus or cotransfection with a plasmid which expressed the adenovirus translational control RNA, VA1 RNA. Cotransfection with plasmids containing the gene for VA1 RNA resulted in elevated levels of CAT activity. VA1 RNA stimulated translation of the chimeric mRNA. However, in two cases, the VA1 RNA apparently decreased the level of mRNA. These results suggest that in addition to its function in translation, VA1 RNA acts at a second site to alter cytoplasmic accumulation of some mRNAs. Infection with adenovirus increased CAT activity several-fold by increasing the cytoplasmic levels of the chimeric AAV-CAT transcript. When the CAT gene is inserted down stream of the AAV intron, adenovirus and not VA1 RNA alone increased CAT activity by promoting accumulation of a spliced transcript.

9/7/31
DIALOG(R)File 155:MEDLINE(R)

05368677 88288213
Cloning of the human thyrotropin beta-subunit gene and transient expression of biologically active human thyrotropin after gene transfection.
Wondisford FE; Usala SJ; DeCherney GS; Castren M; Radovick S; Gyves PW; Trempe JP; Kerfoot BP; Nikodem VM; Carter BJ; et al
Molecular, Cellular and Nutritional Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland 20892.
Mol Endocrinol (UNITED STATES) Jan 1988, 2 (1) p32-9, ISSN 0888-8809 Journal Code: NGZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A 17 kilobase pair fragment of DNA containing the human TSH (hTSH) beta-subunit gene was isolated from a human leukocyte genomic library. Using a 621 base pair human CG alpha-subunit cDNA and a 2.0 kilobase pair genomic fragment of hTSH beta containing both coding exons, we constructed hCG alpha and hTSH beta expression vectors containing either the early promoter of simian virus 40 or the promoters of adeno-associated virus.

Cotransfection of two adeno-associated virus vectors, each containing one subunit of hTSH, together with a plasmid containing the adenovirus VA RNA genes produced hTSH as well as free human alpha- and TSH beta-subunits in an adenovirus transformed human embryonal kidney cell line (293). The levels of protein expression in this system were 10- to 100-fold greater than that found in a simian virus transformed monkey kidney cell line (COS) using vectors containing the early promoter of simian virus 40. The hTSH synthesized in 293 cells was glycosylated as indicated by complete binding to concanavalin A-Sepharose but was larger in apparent molecular weight than a standard hTSH preparation on gel chromatography suggesting an altered glycosylation pattern. However, it was immunologically and biologically indistinguishable from two pituitary hTSH standards in an immunoradiometric and in vitro iodide trapping assay, respectively.

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S6 5 S5 NOT S1
S7 17783 PROMOTER OR PROMOTERS
S8 16 S3 AND S7 NOT S1
S9 16 S8 NOT S6
S10 0 EXPRESSION(1A)CONTROL?
S11 2028 EXPRESS?(2N)CONTROL?
S12 0 S11 AND S2 NOT (S1 OR S6 OR S9)
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0144085 DBA Accession No.: 93-02137
Status of ribozyme and antisense-based developmental approaches for anti-HIV-1 therapy - adeno-associated virus vector for antisense DNA and antisense RNA expression for HIV virus-1 gene therapy (conference paper)
AUTHOR: Zaia J A; Chatterjee S; Wong K K; Elkins D; Taylor N R; Rossi J J
CORPORATE SOURCE: Division of Pediatrics, City of Hope National Medical Center, Duarte, California 91010-0269, USA.
JOURNAL: Ann.N.Y.Acad.Sci. (660, 95-106) 1992
CODEN: ANYAA9
LANGUAGE: English
ABSTRACT: The adeno-associated virus (AAV) may be a candidate vector for use in virucide gene therapy. Antisense DNA and RNA have been shown to inhibit HIV virus-1 as either synthetic DNA or expressed RNA (intracellular immunization). Systems are being developed for inserting into the host cell genome the DNA sequences that could potentially confer resistance to HIV virus replication. A modified vector system based on the nonpathogenic, replication-defective parvo virus AAV. AAV directs the stable integration of foreign DNA encoding an HIV virus-1-specific antisense RNA. The target for the antisense RNA-transcript is the TAR sequence (a cis-acting RNA stem-loop structure in the HIV virus-1 long terminal repeat). The targeted region, TAR, is highly conserved between HIV virus-1 and SIV virus. Antisense-expressing clonal cell lines were tested for their ability to restrict both HIV virus-1 and SIV replication. Both HIV virus-1 and SIV production were inhibited in the antisense clones, SIV to a lesser degree than HIV virus-1. There was 85% inhibition of SIV replication in clone IIC4 and 92% inhibition of HIV on day 3 postransfection. (69 ref)

6/7/2
DIALOG(R)File 357:Derwent Biotechnology Abs

0138156 DBA Accession No.: 92-10648
Development of recombinant adeno-associated viruses that harbor human beta-globin cDNA/gene towards gene therapy of hemoglobinopathies - adeno-associated virus vector plasmid pAV-delta-KhbG construction and expression in 293, KB and K562 cell culture (conference abstract)
AUTHOR: Ohi S; Webb M S; Sitaric S
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: Miami Short Rep. (1, 116) 1991
CODEN: 9999Y
LANGUAGE: English
ABSTRACT: Recombinant adeno-associated virus-2 (AAV2) vectors harboring human beta-globin (hbG) cDNA were constructed. Chimeric plasmid pAVhbG-psi-1 was constructed as previously described. Plasmid pAV-delta-KhbG was constructed by inserting a full-length hbG cDNA into pAV2-delta-K. The recombinant virus was produced by transfecting the chimeric plasmid into 293 cells together with plasmid pAV2 and AAV2, and preparing the cell lysate at 48 hr post-infection. Upon transfection into 293 cells, the recombinant AAV2 DNA harboring hbG cDNA was rescued from the plasmid and replicated in the cells. This in turn resulted in the production of infectious recombinant AAV. AVhbG-psi-1 expressed mRNA in the virus-infected 293, KB and K562 cells. The second recombinant virus, AV-delta-KhbG expressed hbG protein in the infected 293 cells. To make the expression of hbG cDNA/gene specific to erythroid cells, the erythroid-specific 5'-enhancer elements, DCR/LAR, were spliced into the genome of the recombinant virus. (3 ref)

6/7/3
DIALOG(R)File 357:Derwent Biotechnology Abs

0134768 DBA Accession No.: 92-07260
Gene transfer in human lymphocytes using a vector based on adeno-associated virus - B-lymphocyte, T-lymphocyte transformation using AAV/neo vector, which may be useful in gene therapy
AUTHOR: Muro-Cacho C A; Samulski R J; +Kaplan D
CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, 2085 Adelbert Road, Cleveland, OH 44106, USA.
JOURNAL: J.Immunother. (11, 4, 231-37) 1992
CODEN: 5592H
LANGUAGE: English
ABSTRACT: The inverted terminal repeats of adeno-associated virus (AAV), which mediate integration at a specific site in human chromosome-19, were used to establish a vector for gene transfer into human lymphocytes. Epstein-Barr virus-transformed B-lymphocyte JY cells were infected with vector AAV/neo containing the neomycin-resistance gene and AAV inverted terminal repeats in place of the AAV coding region. A neomycin-resistant cell was isolated after 4 wk in the presence of G418. Non-transformed T-lymphocyte CAN.1 was infected with AAV/neo during cloning. While uninfected CAJ0-10 cells (control) showed a marked reduction in proliferative activity in the presence of G418, transformed CAN.1 was not affected. There were no detectable alterations in the functional properties of CAN.1. Rescue and replication of wild-type AAV occurred with AAV super-infection. However, the vector was not rescued and did not replicate, indicating the stability of the integrated vector and demonstrating an additional level of safety incorporated in its construction. An AAV vector may be a viable alternative to retro viruses for gene therapy in lymphocytes. (32 ref)

6/7/5
DIALOG(R)File 357:Derwent Biotechnology Abs

0086365 DBA Accession No.: 89-04356 PATENT
Stable and viable recombinant animal cell virus vector construction - by contacting Cre with a virus vector containing a lox site and circular DNA containing a lox site
PATENT ASSIGNEE: Du-Pont 1989
PATENT NUMBER: EP 300422 PATENT DATE: 890125 WPI ACCESSION NO.: 89-025608
(8904)
PRIORITY APPLIC. NO.: US 77145 APPLIC. DATE: 870721
NATIONAL APPLIC. NO.: EP 88111596 APPLIC. DATE: 880719
LANGUAGE: English
ABSTRACT: A method for preparing a stable and viable recombinant virus vector for animal cells by site-specific insertion of a DNA fragment into a virus vector comprises: (1) contacting Cre with a 1st lox site, which has been introduced into the DNA of the animal cell virus vector; and (2) contacting Cre with a 2nd lox site in a separate DNA molecule, which is circular so that Cre effects recombination of the circular DNA with the virus vector DNA at the 1st lox site. The initial virus vector preferably contains a selectable marker gene. The DNA fragment preferably lacks the selectable marker. The 1st lox site is introduced into a nonessential region of the vector, e.g. the gIII gene of pseudorabies virus. The DNA fragment preferably encodes a structural protein, an enzyme, a regulatory molecule, or a fragment of any of these. Each of the lox sites is preferably a loxP or a loxC2 site and the vector is preferably SV40, pseudorabies virus, polyoma virus, an adeno virus, an adeno-associated virus, herpes virus, vaccinia virus, cattle papilloma virus, Epstein-Barr virus, a baculo virus or a retro virus, especially RPV42. (19pp)

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Set	Items	Description
S1	84703	PY=1993:1999
S2	504	AAV OR ADENO(W)ASSOCIATED
S3	504	S2 OR ADENOASSOCIATED
S4	44778	SPECIFIC?
S5	140	S3 AND S4
S6	5	S5 NOT S1
S7	17783	PROMOTER OR PROMOTERS
S8	16	S3 AND S7 NOT S1
S9	16	S8 NOT S6
S10	0	EXPRESSION(1A)CONTROL?
S11	2028	EXPRESS?(2N)CONTROL?
S12	0	S11 AND S2 NOT (S1 OR S6 OR S9)

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9/7/1
DIALOG(R)File 357:Derwent Biotechnology Abs
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0140400 DBA Accession No.: 92-12892 PATENT
New adeno-associated virus-2 hybrid gene vector - for foreign gene integration and DNA rescue in mammal cell culture using a helper virus, e.g. plasmid ins 96/lambda-M
PATENT ASSIGNEE: Univ.Florida-Res.Found. 1992
PATENT NUMBER: US 5139941 PATENT DATE: 920818 WPI ACCESSION NO.: 92-299352 (9236)
PRIORITY APPLIC. NO.: US 785224 APPLIC. DATE: 911025
NATIONAL APPLIC. NO.: US 785224 APPLIC. DATE: 911025
LANGUAGE: English
ABSTRACT: A new hybrid gene vector (capable of transduction of foreign DNA into a mammal cell in the presence of a promoter other than an adeno-associated virus (AAV) transcription promoter) comprises foreign DNA ligated into an AAV-2 genome, in place of or in addition to the cap, lip or rep coding sequence or an AAV sequence excluding the 1st and last 145 bp. The AAV genome is cloned in a prokaryotic or yeast plasmid or phage vector (e.g. plasmid pBR322), and may be the entire AAV DNA or a deletion mutant (e.g. dl52-91 or dl3-94), capable of replication on infection of the mammal cell when complemented in trans by an AAV gene. Methods of transducing foreign DNA into mammal cells by infection of cells with the vector, and methods of rescuing foreign DNA from transduced cells by infection with a helper virus (e.g. plasmid ins 96/lambda-M) containing genes for replication of the AAV genome or production of AAV, are also new. The vector may be used for reliable insertion of foreign DNA into mammal cells, so that the transferred genetic material is stable with respect to the insertion locus, and which is susceptible to expression and rescue. (12pp)

9/7/3
DIALOG(R)File 357:Derwent Biotechnology Abs
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0128750 DBA Accession No.: 92-01242
Construction and expression of a recombinant adeno-associated virus that harbors a human beta-globin-encoding cDNA - potential use in gene therapy of thalassemia or sickle cell anemia; gene cloning in KB, K562 and 293 cell culture; vector construction
AUTHOR: Dixit M; Webb M S; Smart W C; +Ohi S
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, 1005 D.B. Todd Jr. Blvd., Nashville, TN 37208, USA.
JOURNAL: Gene (104, 2, 253-57) 1991
CODEN: GENED6
LANGUAGE: English
ABSTRACT: With the goal of using recombinant adeno-associated virus (AAV) for gene therapy of hemoglobinopathies, plasmid pAVh-beta-G-psi-1 was constructed previously, with a human beta-globin cDNA (HBB) gene downstream from the P40 promoter of AAV-2 DNA. Transfection of a 293 cell culture with the plasmid resulted in expression of HBB at the mRNA level, and rescue and replication of the recombinant AAV genome. The replicated recombinant DNA was packaged into an intact virion by trans-complementation with plasmid pAV2 or defective helper plasmids (plasmid pAV-delta-Bam or plasmid pAVXB). The recombinant virus could be isolated by equilibrium cesium chloride density gradient centrifugation, at a density of 1.4 g/cu cm. The defective helpers were used to produce wild-type AAV-free recombinant AAV. The recombinant AAV was infectious, and produced chimeric mRNA containing the HBB sequence in virus-infected 293, KB (oral epidermoid carcinoma) and K562 (human erythroleukemia) cells. These results may be useful in designing strategies for gene therapy of thalassemia or sickle cell anemia. (29 ref)

9/7/4
DIALOG(R)File 357:Derwent Biotechnology Abs
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0124445 DBA Accession No.: 91-12087 PATENT
New adeno-associated virus-derived eukaryotic vector - containing heterologous DNA for protein expression or especially down-regulation of target e.g. HIV virus-1 or herpes simplex virus-1 gene; intracellular immunization and gene therapy
PATENT ASSIGNEE: Nat.Inst.Health-Bethesda 1991
PATENT NUMBER: US 7527195 PATENT DATE: 910702 WPI ACCESSION NO.: 91-237708 (9132)
PRIORITY APPLIC. NO.: US 527195 APPLIC. DATE: 900523
NATIONAL APPLIC. NO.: US 527195 APPLIC. DATE: 900523
LANGUAGE: English
ABSTRACT: Adeno-associated virus (AAV)-based eukaryotic vectors, and cells

transfected with these vectors, are new. The vectors are free of AAV coding sequences and consist of: (a) endogenous cis-active DNA for AAV DNA replication, encapsidation and host cell replication; (b) endogenous AAV polyadenylation signal; (c) a promoter; and (d) a heterologous DNA fragment, operably linked to (b) and (c) and present in the sense or antisense direction. The heterologous DNA fragment can encode a foreign protein or viral component. Specified AAV-based eukaryotic vectors (e.g. CWRSV:HIV-ASN and CWRSV:SN) confer intracellular resistance to HIV virus-1 and herpes simplex virus-1 (HSV-1) infection. The vectors can be used to down-regulate a targeted viral (HIV-1, HSV-1) or cellular (histocompatibility gene involved in graft rejection) gene of known sequence, or for protein expression. In a preferred process, the AAV-based vectors are used to produce an antisense mRNA complementary to a 5'-noncoding region of the primary HIV-1 RNA transcript including the core TAR sequence. The mRNA inhibits HIV-1 replication and infectious particle production. (69pp)

9/7/5
DIALOG(R)File 357:Derwent Biotechnology Abs

0110288 DBA Accession No.: 90-12979
Construction of recombinant adeno-associated virus that harbors human beta-globin cDNA - vector construction for potential application in hemoglobinopathy gene therapy; gene cloning and expression in 293 cell culture (conference abstract)
AUTHOR: Ohi S; Dixit M; Tillery M K; Plonk S G
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: J.Cell.Biochem. (Suppl.14A, D422) 1990
CODEN: JCEBD5
LANGUAGE: English
ABSTRACT: The possibility of developing human recombinant parvo virus vectors containing normal alpha-globin or beta-globin cDNA genes for gene therapy of hemoglobinopathies was investigated. The human beta-globin cDNA was excised from JW102 using S1-nuclease and ligated with adeno-associated virus-2 (AAV2) DNA in plasmid pAV2, downstream of the P40 promoter. Cloning of this construct in Escherichia coli DH5 resulted in isolation of recombinant plasmid pAVHbetaGHP11. Transfection via electroporation into human 293 cell culture resulted in expression of the beta-globin cDNA, as evidenced by biosynthesis of transcripts hybridizing to a human beta-globin cDNA probe. Addition of the 3'-end region of AAV DNA containing both a transcription termination signal and the replication origin for AAV to plasmid pAVHbetaGHP11 resulted in production of plasmid pAVHbetaGpsi1. Transfection of this construct into 293 cells permitted the recombinant AAV DNA containing the beta-globin cDNA to replicate inside the cell. This, in turn, resulted in production of the infectious recombinant virus. (0 ref)

9/7/6
DIALOG(R)File 357:Derwent Biotechnology Abs

0110266 DBA Accession No.: 90-12957
Construction and replication of an adeno-associated virus expression vector that contains human beta-globin cDNA - plasmid pAVh-beta-GHP11 and plasmid pAVh-beta-G-psi-1 construction; potential application in gene therapy of e.g. sickle cell anemia or thalassemia
AUTHOR: Ohi S; Dixit M; Tillery M K; Plonk S G
CORPORATE SOURCE: Department of Biochemistry, Meharry Medical College, 1005 D.B. Todd Jr. Blvd., Nashville, TN 37208, USA.
JOURNAL: Gene (89, 2, 279-82) 1990
CODEN: GENED6
LANGUAGE: English
ABSTRACT: With the goal of using an adeno-associated virus (AAV) as a gene transfer vector for gene therapy of hemoglobinopathies (e.g. sickle cell anemia or thalassemia), human beta-globin cDNA was ligated downstream from the P40 promoter of the AAV-2 genome. To circumvent difficulties of cloning DNA containing palindromic sequences, 2 of which exist in the termini of the AAV genome, a stepwise approach handling 1 palindrome at a time was devised to construct a chimeric expression vector, plasmid pAVh-beta-GHP11. Electroporation of the construct into a human 293 cell culture resulted in expression of the cloned human beta-globin cDNA, as evidenced by the biosynthesis of transcripts hybridizable to a human beta-globin cDNA probe. Addition of the 3'-end region of AAV DNA containing both the transcription termination signal and DNA replication origin for AAV to the construct (to give plasmid pAVh-beta-G-psi-1) permitted the recombinant AAV genome to be rescued and replicate in the cell. (17 ref)

9/7/7
DIALOG(R)File 357:Derwent Biotechnology Abs

0106673 DBA Accession No.: 90-09364
Production and expression of recombinant adeno-associated viruses harboring human beta-globin cDNA - adeno-associated virus expression in 293 cell culture; potential gene therapy for hemoglobinopathy diseases (conference abstract)
AUTHOR: Ohi S; Dixit M; Plonk S G
CORPORATE SOURCE: Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: FASEB J. (4, 7, A2288) 1990
CODEN: FAJOEC
LANGUAGE: English
ABSTRACT: 2 Plasmids that harbor human beta-globin (hbG) cDNA downstream of the P40 promoter of adeno-associated virus-2 (AAV2) DNA were

constructed with the aim of using recombinant human parvo virus for hemoglobinopathy gene therapy. Plasmid pAVhbetaGpsil contains a partial hbG cDNA derived from JW102, whereas plasmid pAVdeltaKhbG contains a full-length hbG cDNA derived from plasmid pB6-6. Upon transfection, pAVhbetaGpsil expressed chimeric RNAs containing hbG sequences in human 293 cells. Recombinant genomes were rescued from both plasmids and replicated in the cell. This led to the production of infections recombinant AAV. When infected in 293 cells, the virus preparation resulted in efficient expression of hbG mRNAs in the cell. (3 ref)

9/7/9
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0086328 DBA Accession No.: 89-04319
Construction and characterization of recombinant adeno-associated virus genome containing human beta-globin cDNA - gene cloning and expression in human cell culture; potential sickle cell anemia or thalassemia gene therapy (conference abstract)
AUTHOR: Ohi S; Dixit M; Tillery M K
CORPORATE SOURCE: Department of Biochemistry and the Sickle Cell Center, Meharry Medical College, Nashville, TN 37208, USA.
JOURNAL: J.Cell Biol. (107, 6, Pt.3, 304a) 1988
CODEN: JCLBA3
LANGUAGE: English
ABSTRACT: The human parvo virus, adeno-associated virus, is a useful vector for cloning and expression of foreign genes. With the aim of construction of recombinant human parvo viruses containing either alpha-globin or beta-globin genes for gene therapy of hemoglobinopathies, such as sickle cell anemia and thalassemia, a cDNA sequence for human beta-globin was isolated and inserted downstream of the p40 promoter of adeno-associated virus. The beta-globin cDNA was excised from plasmid JW102 using S1 nuclease. The fragment was treated with Escherichia coli DNA-polymerase-I (EC-2.7.7.7), Klenow fragment and blunt-end ligated to plasmid pBR322, followed by cloning in Escherichia coli HB101. 1 Clone, plasmid pHbetaGS3, was amplified and the intact beta-globin cDNA region was excised on a HindIII-NhiI fragment. The fragment was treated with Bal31 and blunt-end ligated to plasmid pAV2 downstream of the p40 promoter (HindIII site). From plasmid pAV2 a KpnI fragment was deleted (plasmid pAVdeltaKpn) to accommodate the foreign DNA. Expression of beta-globin under the control of p40 promoter was tested in human 293 cell culture and pluripotent K562 cell culture. (2 ref)

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DIALOG(R)File 357:Derwent Biotechnology Abs
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0082125 DBA Accession No.: 89-00116
Expression and rescue of a nonselected marker from an integrated AAV vector - chloramphenicol-acetyltransferase gene cloning in human cell culture using adeno-associated virus vector
AUTHOR: Mendelson E; Smith M G; Carter B J
CORPORATE SOURCE: Laboratory of Molecular and Cellular Biology, National Institute of Diabetes, Digestive, and Kidney Diseases, Building 8, Room 304, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Virology (166, 1, 154-65) 1988
CODEN: VIRLAX
LANGUAGE: English
ABSTRACT: Rep+ and rep- adeno-associated virus (AAV) vectors (plasmid pEM15 and plasmid pEM612 respectively) were constructed, containing a chloramphenicol-acetyltransferase (EC-2.3.1.28) (CAT) gene driven by the AAV p40 promoter, and a neo gene, driven by a herpes virus thymidine-kinase (EC-2.7.1.21) gene promoter. The vectors were transfected into a human 293 cell or HeLa cell culture, geneticin-resistant cells were selected, and cells were screened for CAT expression. With 293 cells, most rep- clones showed high CAT expression, but only 50% of rep+ clones expressed CAT, at a low level. With HeLa cells 25% of rep+ and rep- clones expressed CAT, some rep+ clones giving high yields. The rep+ vectors were also analyzed by rescue after superinfection with adeno virus and by Southern blot. AAV-CAT DNA could be rescued from 50% of HeLa cells but not from 293 cells. Non-rescue could be due to rearrangement of AAV termini or the rep gene. Western blot analysis showed low constitutive expression of rep protein in 1 293 cell clone and 2 HeLa cell clones. Thus, the AAV p40 promoter could drive expression of non-selected markers in integrated vectors, which could then be rescued. (26 ref)
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